SUMMER 1993

NIH NEWS & FEATURES

NATIONAL INSTITUTES OF HEALTH

NIH Adds Institutes on Mental and Addictive Disorders

National Institutes of Health
Department of Health
and Human Services

NIH NEWS & FEATURES

NATIONAL INSTITUTES OF HEALTH

Special Section

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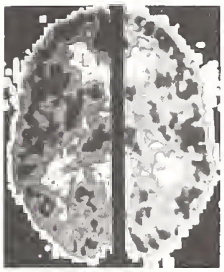

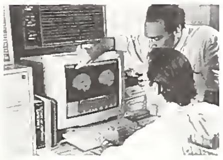

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EDITOR
MARY SULLIVAN

GRAPHIC DESIGN
RICHARD BARNES

OFFICE OF COMMUNICATIONS
PUBLIC INFORMATION BRANCH
BUILDING 31, ROOM 2B-10
9000 ROCKVILLE PIKE
BETHESDA, MD 20892
(301) 496-1766

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COVER DESIGN: BACKGROUND IS A COMPUTER MODEL OF A COCAINE MOLECULE. SEE SPECIAL SECTION FOR INFORMATION ON PHOTOS.

NIH's "Basic Research" Institute Turns 30

In 1962, when the NIH Division of General Medical Sciences became the National Institute of General Medical Sciences (NIGMS), researchers were just beginning to learn how DNA directs the production of proteins. It was less than 10 years since the publication by James Watson and Francis Crick of the paper that described, for the first time, the structure of the DNA molecule.

The main mission of the new institute was the support of basic research. In the Institute's first 10 years, its grantees discovered restriction enzymes, which permitted scientists to cut DNA at specific places. Other NIGMS grantees were instrumental in the discovery of ligase, which made it possible to "stick together" spliced pieces of DNA.

These "cutting and pasting" tools, in turn, permitted the development of recombinant DNA technology, which has revolutionized biomedical science. Not only are researchers today able to ask questions undreamed of before the technology was developed, but also many direct clinical benefits, such as gene therapy for some diseases, are now beginning to be realized.

By the 1980's, recombinant DNA technology had formed the basis of the rapidly growing biotechnology industry, and the first drugs produced by these techniques, including human insulin and human growth hormone, had appeared on the market. Ten years later, 11 medicines that were produced through biotechnology were available to physicians, and more than 100 additional "biotech" drugs and vaccines were in various stages of the testing and approval process.

By laying the foundations for this important new industry, NIGMS-supported basic research has resulted in direct economic benefits. Many industries outside the realm of medicine, such as agriculture and food processing, have also benefitted from the application of biotechnology, and the potential for future applications is tremendous.

Over the years, the research supported by NIGMS has often resulted in the discovery of fundamental principles that shape the way scientists approach the problems of disease. One indication of the significance of this research is the fact that over half of the NIH-supported Nobel Prize winners have received grants from NIGMS.

"Science has made amazing strides in the past 30 years," notes Dr. Ruth L. Kirschstein, who recently moved from her position as Director of the National Institute of General Medical Sciences, to become Acting Director, NIH, "but, today, the need for a basic research institute is just as great as—or perhaps greater than—it was in 1962, because much still needs to be learned about how basic biological systems work before we can understand how to correct many disorders."

NIGMS has no laboratories on the NIH campus. With the exception of a small intramural training program, the research and research training activities

"Science has made amazing strides in the past 30 years," notes Acting NIH Director Dr. Ruth Kirschstein, "but, today, the need for a basic research institute is just as great as—or perhaps greater than—it was in 1962..."

supported by the Institute take place at universities, medical schools, hospitals, and research institutions throughout the country.

DNA AND RNA

In the 30 years that NIGMS has been an institute, basic researchers have uncovered many surprises about DNA and RNA. They have found introns that make up large sections of the genes of higher organisms and that do not code for proteins. They have found DNA segments, called transposable elements, which spontaneously move from one location to another. A recent study showed that movement of a transposable element is involved in a genetic disease, in this case, hemophilia.

Micrograph of DNA condensed in a chromosome.

Scientists are also finding that RNA is not just a passive transmitter of information from the DNA, but is much more complex than they previously thought. In the early 1980's, NIGMS grantees (who later received the Nobel Prize for this work) showed that certain RNA molecules possess catalytic activity—that is, they can perform the enzyme-like function of speeding up chemical reactions. This unexpected finding has revolutionized research on RNA. Scientists are now working with catalytic RNA molecules, called ribozymes, to see if they can be engineered to perform various useful functions, including the destruction of harmful viruses. Initial attempts to create these "designer" ribozymes have been encouraging.

CELL STUDIES

NIGMS supports research in a wide range of scientific areas. Most of this research is administered within four program branches: Cellular and Molecular Basis of Disease, Genetics, Pharmacology and Biorelated Chemistry, and Biophysics and Physiological Sciences. However, there is often cross-fertilization in the research supported by these branches. A particularly striking example can be found in the field of cell cycle research.

Although geneticists and cell biologists originally approached cell cycle studies from different directions, their work has converged and is now shedding light on processes of normal and abnormal development and growth, including cancer. Clinical benefits are now beginning to result from this merging of years of research in basic cell biology

Dr. Ruth L. Kirschstein, who recently moved from her position as Director of the National Institute of General Medical Sciences, to become Acting Director, NIH.

with studies of cancer biology, immunology, developmental biology, and hematology.

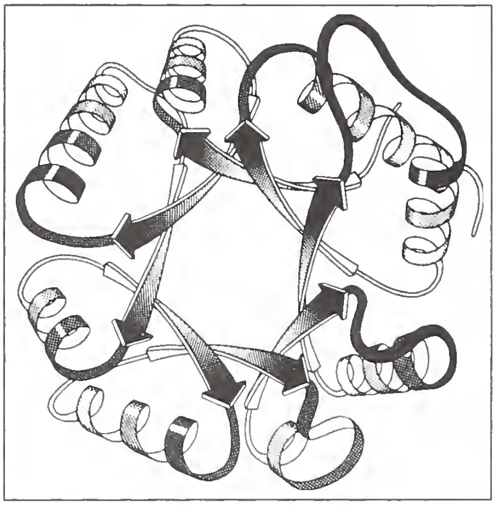
For decades, cell biologists studied the fundamental mechanisms of cell adhesion. It was hoped that this work would shed light on such questions as why cells either stick together too well—causing the chronic inflammation seen in diseases like arthritis—or don't stick together well enough—a process that enables cancer cells to slip away from the primary site and metastasize. But first, the scientists needed to build a body of knowledge by isolating and carefully characterizing the molecular mechanisms involved.

Now, this research has advanced to the drug development stage. One of the first drugs, which enhances cell adhesion and thus is designed to speed wound healing, is in the approval process at the Food and Drug Administration. Other drugs are being developed to treat shock and to prevent bits of broken-up blood clots from causing further clots. Eventually, biotech companies may be able to develop drugs to prevent the metastasis of cancer cells.

BIORELATED CHEMISTRY

NIGMS supports the bulk of the NIH-funded basic research in chemistry, especially those studies aimed at the total synthesis of natural products. One such product is the promising anticancer drug taxol, which is currently derived from yew trees. Because each yew tree yields only a small amount of taxol and because the trees are in limited supply, scientists are racing to find ways to synthesize this compound in the laboratory. Many of the techniques that they are using were developed by NIGMS grantees.

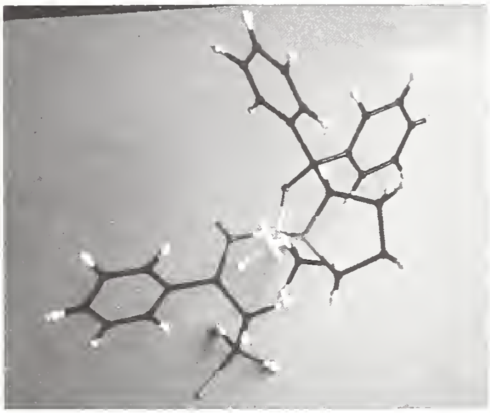
Interestingly, much of the current attention to taxol was stimulated by basic research done by an NIGMS grantee in the late 1970's, which showed that this drug works by interfering with the normal breakdown of microtubules. These structures have an important role in cell division, cell movement, and the transport of substances within the cell. Once taxol's mechanism of action was found, its potential use as a cancer chemotherapeutic agent became clear, and the National Cancer Institute began sponsoring studies using taxol.



A schematic diagram of a protein structure obtained through x-ray crystallography. *(Courtesy of Dr. David Richardson and Jane Richardson)*

Studies in basic chemistry affect all areas of biomedical research. These studies aim to uncover the chemical patterns and rules that underlie the functioning of biological molecules. Understanding these rules can lead to new synthetic substances that are able to carry out delicate chemical transformations. One goal of chemists is to learn how to "engineer" enzymes to provide greater control over chemical reactions, prevent the synthesis of unwanted byproducts, and produce drugs more quickly and less expensively than is now possible.

An example of this work is the invention of molecules called "chemzymes" by a Nobel Prize-winning NIGMS grantee. The first chemzymes that have been produced are designed to help eliminate one of the most persistent roadblocks to efficient, cost-effective chemical synthesis: the creation of a product that is a mixture of molecules having two different spatial orientations. Molecules of only one of the orientations are needed to perform the desired task and, while the opposite form may have no effect, often it can cause adverse reactions ranging from mild to serious. For example, the severe birth defects caused by the drug thalidomide have been attributed to the opposite form of the therapeutic molecule. The ability of chemzymes to make every molecule of a product in the same biologically effective orientation could have an important impact on the pharmaceutical industry, as well as on basic research.



A model of a chemzyme taking part in a chemical reaction. This particular reaction can produce fluoxetine, a drug that may be useful in treating depression, chronic pain, and eating disorders.

BIOPHYSICS AND THE STRUCTURE OF MOLECULES

Another area in which NIGMS plays a pivotal role is the support of research that determines molecular structures at very high resolution. Much of our current understanding of the detailed mechanisms by which large biological molecules function has come from the techniques of structural biology, such as x-ray crystallography and nuclear magnetic resonance spectroscopy.

Scientists seek to determine the structures of biologically important molecules like DNA, RNA, and proteins because, to a large extent, a molecule's structure determines how it functions. Since it is not possible to "read" amino acid sequences in such a way as to predict the detailed three-dimensional structure of large molecules, researchers use a variety of special techniques to arrive at this information. These techniques—including x-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy—have improved considerably in recent years, enabling scientists to decipher structures rapidly and more precisely. In addition, faster and less expensive computers are giving researchers new ability to handle enormous quantities of data and—through computer graphics—to visualize the structures and movements of proteins.

NIGMS-supported studies of the structure of the proteins of the human immunodeficiency virus (HIV) have led to a number of important achievements, including the determination of the detailed structure of an enzyme, reverse transcriptase, that is essential to the HIV life cycle; the structure of the part of the receptor protein through which HIV infects the body; and a new method for the identification of compounds that might bind to, and thus inhibit, HIV.

TOOLS FOR RESEARCH

In the course of their studies, NIGMS grantees frequently develop new research tools. Often, these tools are spin-offs from research that began as an attempt to understand some basic principle. For example, NIGMS-supported studies on genetic mechanisms led to the recent ability to create mice in which a specific gene has been inactivated. These so-called "knockout" mice are already being used in research on genetic disorders, most notably cystic fibrosis, where they represent the first animal model for this disease. The mice have also been used in studies on normal development, immunology, and learning and memory.

RESEARCH TRAINING AND MINORITY RESEARCH PROGRAMS

Since the inception of NIGMS, the support of research training has been a vital part of its mission. Well-trained scientists are the most critical component of any research laboratory. At present, nearly half of all the NIH predoctoral trainees, as well as many postdoctoral trainees, receive their support from NIGMS.

The Institute is also dedicated to increasing the number of minority biomedical scientists. Toward this end, NIGMS sponsors special research and research training programs for students and faculty members at institutions with substantial minority enrollments through the Minority Biomedical Research Support Program and the Minority Access to Research Careers Program. These programs have helped thousands of minority students pursue undergraduate and graduate degrees and have enhanced research and research training activities at minority institutions.

THE FUTURE

In reflecting on the Institute's 30th anniversary, Dr. Kirschstein says, "NIGMS is proud to have contributed to the 'biological revolution' of the past few decades. We look forward now to being able to build on this beginning, to further develop our understanding of fundamental life processes so that we will be able to prevent, treat, and cure many of the diseases that still evade our control." ▲

—Doris Brody, public affairs specialist, NIGMS.

Jacqueline Barton: Spelling Out the ABZ of DNA

When Jacqueline Barton, Ph.D., now a professor at the California Institute of Technology in Pasadena, California and a grantee of the National Institute of General Medical Sciences was in high school, she liked drawing, architecture, and puzzles. She also loved math, especially geometry, but she did not study chemistry. At that time, she says, "girls didn't do that."

It was not until Dr. Barton was an undergraduate at Barnard College that she discovered the "chemistry" between herself and chemistry. She found that studying chemistry reinforced her love of shapes and made it possible for her to ask questions that had "relevance to life processes... When I got in the lab and saw the marvelous colors of chemical reactions taking place in the test tube, I was hooked."

Today, Dr. Barton is using the tools of inorganic chemistry to probe the unexplored regions of various forms of the DNA molecule.

In the most familiar and well-characterized form of the molecule, called B-DNA, the bases pair to resemble the rungs of a ladder.

The sugars and phosphates are like the "side rails" of this ladder. In addition, the B-DNA helix is said to have a "righthanded" twist.

OTHER FORMS OF DNA

But not all DNA is B-DNA. Two other forms, A-DNA and Z-DNA, have been identified. These alternative forms have the same bases, sugars, and phosphates as does B-DNA, but their arrangment in space is different.

Like B-DNA, A-DNA twists into a right-handed helix. However, the distance between successive pairs of bases in A-DNA is smaller than it is in B-DNA, giving A-DNA a squatter appearance.

Z-DNA twists into a left-handed helix and has a zigzagging backbone (hence its name). The base pairs in Z-DNA are tilted differently than are the base pairs in the other two forms, so Z-DNA looks long and slim.

STUDYING THE SHAPE OF DNA WITH METAL COMPLEXES

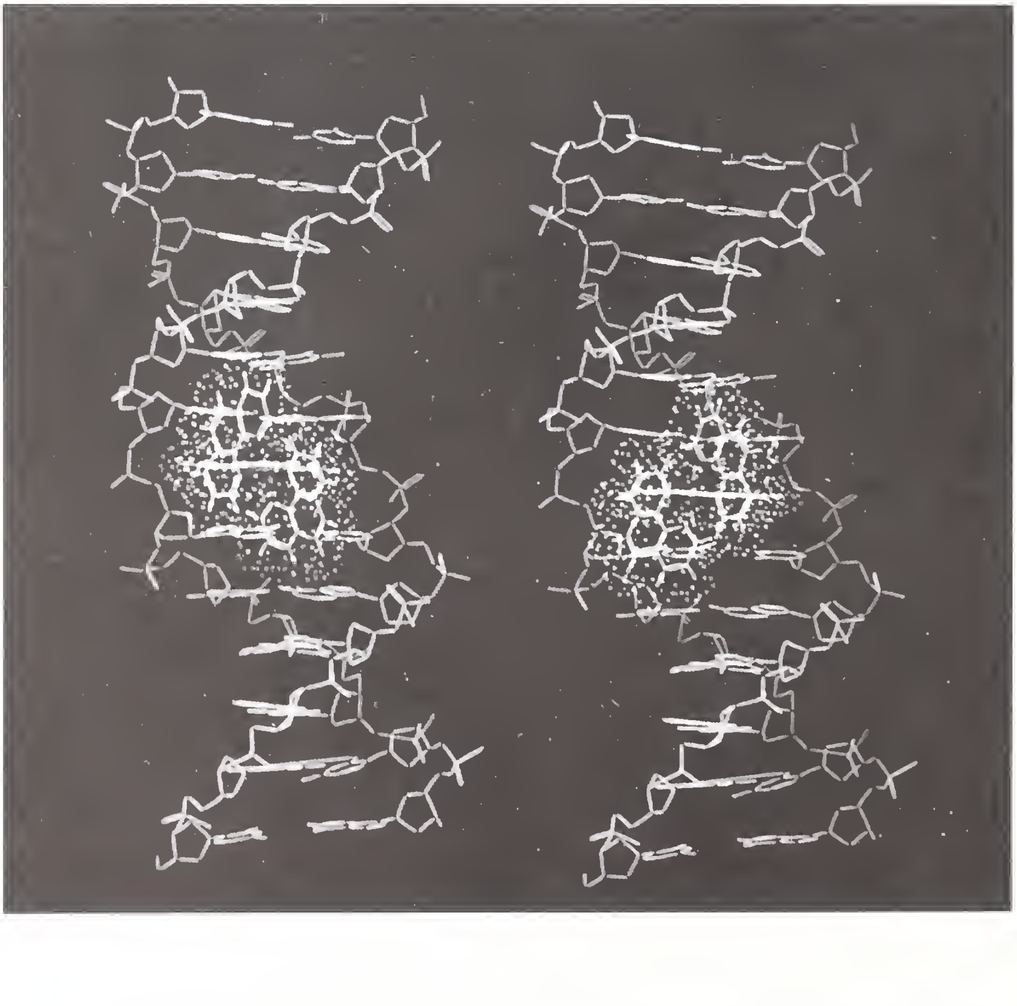
The coded instructions for the manufacture of the body's myriad proteins are stored in the DNA in individual genes, and are read only at certain times in the cell's life cycle. What regulates this process of gene expression? Does the shape of the DNA play a role? Dr. Barton finds this possibility intriguing.

Many studies have shown that proteins called transcription factors regulate gene expression by binding to specific sites on DNA. Binding is dependent upon a proper "fit" between the nooks and crannies of the DNA and those of the protein. Dr. Barton and her colleagues have probed these same grooves and ridges with great precision using metal-containing molecules called metallointercalators.

Dr. Barton began preparing and studying metallointercalators in the mid-1970's, when she was a graduate student in the laboratory of Dr. Stephen Lippard at Columbia University. As an assistant professor at Columbia, she decided to build a three-dimensional version of the two-dimensional complex that was being used for DNA studies at the time. She came up with a "propeller-shaped molecule that had three blades protruding from a central metal ion." The overall shape of the complex was roundish, and she says that "we did not expect it to react with anything." In fact, she adds, "we planned to use this new three-dimensional molecule as a control."

To her surprise, Dr. Barton found that her new complex bound tightly to B-DNA. One of the blades of the propeller actually inserted itself—or intercalated—between two adjacent bases, anchoring the complex to the DNA molecule. The remaining blades nestled into the grooves of the DNA. The two molecules seemed to grip one another like hands engaged in a handshake.

Dr. Barton and her coworkers were subsequently able to produce a panel of metal complexes that selectively bound to A-DNA or to Z-DNA as well. Each metal complex had a "handedness."



Model illustrating the selectivity in binding of transition metal complexes to DNA. Binding of the right-handed propeller shaped molecule (shown on right) to right-handed DNA is preferred over binding of the left-handed isomer (shown on left), because the symmetry of the molecule matches that of the helix.

Though much smaller than the transcription factors, the metal complexes found and paired up with specific bumpy landmarks along the vast stretch of DNA. Because the metal complexes are well characterized and their shapes understood, they reveal important information about the shapes in the DNA.

DNA DRUGS

The first set of metal complexes that Dr. Barton prepared cut right through (when activated by light) the DNA helix at the binding sites. She compares the attachment and cutting by the metal complexes to a "small bomb going off next to the DNA." She notes that, sometime in the future, complexes such as these could prove to be powerful tools for the treatment of cancer. If the DNA in cancer cells can be damaged, their out-of-control growth could be stopped. DNA-cutting drugs that are currently used to treat cancer tend to be very nonspecific, snipping the DNA in many places and harming even healthy cells. If metal complexes can be identified that seek out and attach only to DNA that is directly involved in the development of cancer, the side effects of drug treatment might be greatly reduced. However, Dr. Barton cautions that many technical problems remain to be overcome before such drugs might actually become available.

Dr. Barton's collection of metal complex probes continues to grow. Like sensitive fingers moving over Braille letters, each new complex has helped to decipher the still-secret message contained in DNA's twists and turns. The newest series of complexes fluoresce when they bind to DNA. She says that these glowing, colorful reagents remind her of her first days in the college chemistry lab, and that they also make "great demonstrations in undergraduate chemistry classes." Now, students visiting her laboratory may find that they, like Dr. Barton herself, become hooked on the dazzling colors and shapes of chemistry. ▲

—Anne Oplinger, former technical publications writer, and Ruth Guyer, writer/biological sciences, NIGMS.

Massachusetts Genome Center Uses New Technology to Map Entire Genome

> *"Progress in physical mapping has been greater than we expected in our planning for the human genome project."*
>
> *—Dr. Elke Jordan, NCHGR deputy director.*

The human genome center at the Whitehead Institute for Biomedical Research has geared up to construct low-resolution physical maps of the entire human genome. Physical maps are made by matching up overlapping segments of cloned DNA in order to generate progressively longer sets of DNA pieces, which can represent an entire chromosome.

Since the beginning of the human genome project, researchers have only been able to construct physical maps one chromosome at a time. But the recent development of improved and more automated technologies for generating physical maps has now led the Whitehead researchers to attempt the procedure on all of the 24 different human chromosomes at once.

The National Center for Human Genome Research (NCHGR) is awarding a grant to renew and expand the work of Dr. Eric Lander, Director of the Whitehead Center for Genome Research, and his colleagues. These researchers have already developed and tested techniques for genome-wide mapping when they constructed another type of map, known as a genetic linkage map, covering the entire mouse genome. The new grant, which will total $8.3 million in the first year, will apply these techniques to completing genetic linkage and physical maps of the mouse genome. It will also take advantage of newly developed DNA clones called "mega-YAC's" to construct a low-resolution physical map of the entire human genome.

"Progress in physical mapping has been greater than we expected in our planning for the human genome project," says NCHGR deputy director Dr. Elke Jordan. "It is prudent for us at this time to take full advantage of newly developed mapping technologies to speed the project along so the tools can be delivered to the scientific community as quickly as possible."

Work on both the mouse and human genomes will allow scientists to compare information about the functions of genes in the two species. The mouse genome, for example, is more than 90 percent similar to that of the human, and many regions are essentially identical. Also, most mouse genes carry out functions identical to their counterparts in humans. Relating knowledge from mouse studies to humans depends on the ability to identify and isolate a gene associated with a disease in mice and then looking for that gene's counterpart in humans.

Lander and his colleagues will continue to refine the genetic linkage map of the mouse genome by generating 6,000 DNA sequencebased markers, called simple sequence length polymorphisms (SSLP's), which will be spaced an average of 300,000 base pairs apart. Such a set of markers will allow scientists to quickly locate individual genes and provide them with better tools to tease apart the contributions several genes make to a single trait or disease.

SSLP's from the genetic linkage map will also provide continuity with the physical map of the mouse genome. The Whitehead Center will develop a YAC, or yeast artificial chromosome, library of cloned DNA from the mouse genome and order those clones using 10,000 sequence-tagged sites (STSs). STSs are short, unique stretches of DNA that can be detected by polymerase chain reaction. Because an SSLP can also serve as an STS, they will be used to tie information from the genetic map with that of the physical map. And because physical maps represent actual pieces of cloned DNA, the maps can provide gene hunters with the exact piece that contains their gene, once its location has been flanked by markers on the genetic linkage map.

Genome centers, such as the Whitehead Center, located at institutions around the country, form the nucleus of the National Center for Human Genome Research's (NCHGR) technology development and chromosome mapping activities. Genome centers house mission-oriented, interdisciplinary projects designed to efficiently attack large-scale genome research problems that require unique and creative solutions. New approaches developed and applied in NCHGR genome centers have resulted in high rates of data production and rapid distribution of information to the scientific community.

Human genome centers also play a key role in improving and sharing genome research technology and resources by way of collaboration, public access to laboratory databases, and sponsorship of "visitor laboratories", where visiting scientists gain access and apply genome center expertise and technology to their own research problems. In addition, several centers include outreach programs to clinicians, educators, journalists, and the general public to foster a better public understanding of human genetics as well as genome research. ▲

—Leslie Fink, Information Officer, NCHGR.

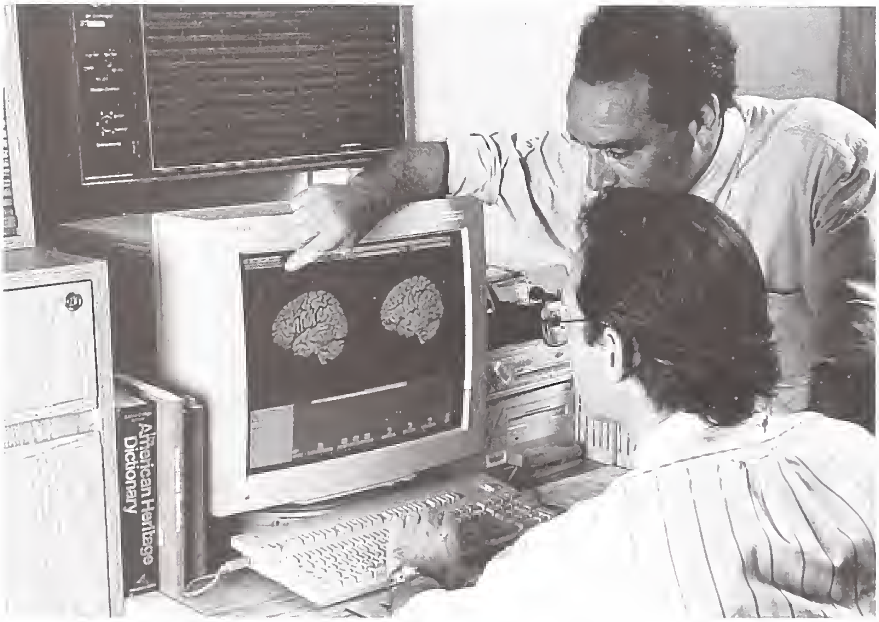
INHERITED DISEASE GENES THAT WERE IDENTIFIED BY TECHNIQUES CURRENTLY IN USE BY NIH'S HUMAN GENOME PROJECT

CHRONIC GRANULOMATOUS DISEASE*	1986
DUCHENNE MUSCULAR DYSTROPHY*	1986
RETINOBLASTOMA	1986
CYSTIC FIBROSIS	1989
WILMS TUMOR	1990
NEUROFIBROMATOSIS TYPE 1	1990
TESTIS DETERMINING FACTOR	1990
CHOROIDEREMIA*	1990
FRAGILE X*	1991
FAMILIAL POLYPOSIS COLI	1991
X-LINKED KALLMANN SYNDROME*	1991
ANIRIDIA	1991
MYOTONIC DYSTROPHY	1992
LOWE SYNDROME*	1992
NORRIE SYNDROME*	1992
MENKES SYNDROME*	1993
X-LINKED AGAMMAGLOBULINEMIA*	1993
GLYCEROL KINASE DEFICIENCY*	1993
ADRENOLEUKODYSTROPHY*	1993
NEUROFIBROMATOSIS TYPE 2	1993
HUNTINGTON'S DISEASE	1993
NON POLYPOSIS COLORECTAL CANCER	1993

*X-linked

NIH Adds Institutes on Mental and Addictive Disorders

In October 1992, the research components of the three institutes of the former Alcohol, Drug Abuse, and Mental Health Administration joined the National Institutes of Health. They are the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The following section is an overview of each institute's research program and special areas of interest.



Drs. Daniel Weinberger and Thomas Noga examine anatomical differences in brains of identical twins discordant for schizophrenia, revealed by 3-D surface renderings reconstructed from 122 MRI (Magnetic Resonance Imaging) slices.

Discoveries in Brain Science Change Public Attitudes About Mental Illness

The recent return of the National Institute of Mental Health (NIMH) to NIH "signals an historic shift in the Nation's view of mental illness, shaped by advances in brain and behavioral research and proven effective treatments" according to NIMH Director Dr. Frederick K. Goodwin.

NIMH's departure from the NIH in 1968 reflected not only the priorities of a then burgeoning services grants program, but also a lingering notion of mental illness as different from "physical" illness. Support for this view has since eroded with identification of brain dysfunctions in serious mental illnesses—schizophrenia, depression, manic-depressive illness, panic and obsessive-compulsive disorders—which afflict more than 15 million Americans each year.

It is now widely recognized that mental illnesses, like most medical problems, involve interactions between biological vulnerabilities and environmental factors.

Research documenting how such interactions occur is having a profoundly destigmatizing effect on victims of mental illness and their families, suggests Goodwin.

"At long last, science is providing solid support for the biopsychosocial approach," adds NIMH Deputy Director Dr. Alan Leshner. Judgmental views of the effects of parenting on the development of severe mental illnesses, such as schizophrenia, have been virtually cast aside in the face of new understanding about the role of multiple factors."

Advances in molecular genetics, computer science, and brain imaging are being brought to bear in assessing the efficacy of pharmacologic and psychotherapeutic innovations.

"Because of the nature of mental illnesses—which involve subtle interactions between cognition and mood, and changes in behavior as a function of environment—we have evolved a sophisticated neuroscience that focuses on integrative and regulatory processes in the brain," says Goodwin.

INTRAMURAL RESEARCH: NEVER REALLY LEFT

For the 900+ scientists and support personnel in NIMH's Intramural Research Program (IRP), the Institute's return to NIH simply makes official the institute's previous arrangement with the NIH. NIMH's in-house research arm never actually left the NIH community. It was jointly administered throughout the Institute's quarter-century sojourn.

The world's largest institution devoted to studies of the brain and mental illness, the IRP encompasses 24 laboratories and branches located on the NIH campus, at the NIH Animal Research Center in Poolesville, and at the NIMH Neuroscience Center at Saint Elizabeths Hospital in Washington D.C. Intramural studies represent about 17% of the Institute's $585.7 million budget.

In the NIH Clinical Center (Building 10), the Institute operates 5 inpatient units, an outpatient clinic, and several laboratories. More than 200 clinical protocols are under way at any given time, exploring such problems as schizophrenia, Alzheimer's disease, serious mood and anxiety disorders, childhood attention-deficit/hyperactivity, dyslexia, and a constellation of other illnesses that range from PMS to AIDS. New drug treatments and novel environmental interventions are under investigation, including bright light and sleep/wake cycle shifts for seasonal and circadian mood disturbances. Studies

Technician Julie Gorey and Dr. Richard Coppola demonstrate new brain SPECT (Single Photon Emission Computed Tomography) scanner for schizophrenia studies at NIMH Neuroscience Center at Saint Elizabeths Hospital.

by Dr. Judith Rapoport are demonstrating that childhood obsessive-compulsive disorder responds to treatment with serotonin-selective medications.

In the new Conte Neuroscience Building (49), a program of transgenic rodent research recently scored the first successful gene "knockout" of a human inherited metabolic disease (Gaucher disease). The Conte Building is also the new home of Dr. Mortimer Mishkin's world renowned neuropsychology lab that is systematically tracing the brain's memory circuits.

NIMH's basic science laboratories in Building 36—heirs to historic neurotransmitter metabolism and mapping experiments by Nobelist Drs. Julius Axelrod, Seymour Kety, Louis Sokoloff, and Seymour Kaufman during the 1950s and 1960s—are using molecular genetics probes to explore intracellular messenger proteins and protein synthesis. Investigations there are revealing how and where in the brain drugs like marijuana act.

Across campus at Wilson House (Bldg. 15K), researchers are exploring how psychopathology in parents may affect children's development. They are turning up clues as to how childhood sexual abuse can predispose for dissociative disorders, such as multiple personalities, in adulthood.

NIMH's Neuroscience Center on the grounds of Saint Elizabeths Hospital in Anacostia incorporates a Neuropsychiatric Research Hospital with three inpatient units devoted to studies of schizophrenia. Investigators are using brain scanners and a brain bank facility in search of clues to structural and functional brain abnormalities seen in patients with this devastating disorder that affects nearly 1 percent of the population, typically in young adulthood. Recent work has focused on identical twins discordant for the illness. A pioneer in brain tissue transplantation, the Neuroscience Center is also home to a program of protein/gene mapping studies.

Studies on the neural basis of familial behavior and frontal cortex functioning are under way at NIMH's Poolesville facilities, site of Dr. Paul MacLean's explorations into the evolution of the mammalian brain.

NIMH Director Dr. Frederick K.

Dr. Jacqueline Crawley tests effects of experimental drugs in rat model of memory loss.

Monkey memory testing in neuropsychology study.

Technician Chris Spurney in NIMH Brain Bank slices brain tissue from schizophrenia victim for autoradiographic analysis.

Goodwin points with pride to the IRP as the "premier" training ground for research psychiatrists, psychologists, and mental illness-related neuroscience disciplines. The program was recently ranked first among neuroscience programs at the NIH in numbers of papers published and in average citations per paper (1986-1990) by the Institute for Scientific Information Science Indicators Data Base. Worldwide it ranked second and third respectively in these categories. NIMH's IRP includes a Nobel Laureate, a Lasker awardee, 7 members of the National Academy of Sciences, and several other major prize recipients.

EXTRAMURAL PROGRAMS: HEADQUARTERED AT PARKLAWN

While they evolved some unique features during the Institute's quarter century absence, NIMH's extramural programs generally parallel those of other NIH Institutes. Grant applications, for example, have always been assigned by the NIH Division of Research Grants.

From administrative headquarters in the Parklawn Building in Rockville, extramural staff manage review of applications and administer some 1,800 grants and contracts supporting research on basic brain and behavior; prevention, diagnosis, and treatment of mental disorders; epidemiology and services delivery systems.

An NIMH-supported multisite Epidemiologic Catchment Area Study has established definitive statistics on rates of mental illnesses. It has revealed that more than 20 percent of the population is affected by a diagnosable mental disorder in a given year, including 9 percent who suffer some disability, and 2.8 percent with severe mental illness.

A recent Institute-supported evaluation has found that empirical studies documenting the success rates of treatments for severe mental illness (60–80%) are well within the range for most successfully treated "physical" disorders. In meeting the challenge of providing credible assessments of behavioral/experiential outcomes of both biological and psychological treatments, the mental illness research

Frederick K. Goodwin, M.D., Director of the National Institute of Mental Health.

field has pioneered development of methodologies such as the controlled trial and other innovations now widely adopted throughout medical science.

NIMH is taking the lead among Federal agencies in developing a Human Brain Project that will use advances in computer technologies to help scientists manage the knowledge explosion in the neurosciences. "Information superhighways" of fiber optic networks will facilitate the standardized sharing of new findings and clinical data. Huge, networked databases will, for example, make accessible cumulative information from the various subfields about a particular brain structure, including images from brain scanning and other mapping methodologies.

The Institute is also nurturing the development of new drugs to treat mental illnesses and conducting public education campaigns on panic disorder and depression. The NIMH has been at the forefront of Federal efforts to educate teachers and schoolchildren about brain science and the role of animal research. ▲

—Jules Asher, public affairs specialist, NIMH.

NIDA Adds Drug Abuse Research to NIH

About 3,500 years ago, an Egyptian scribe documented concerns over the use of opium elixirs that produced hallucinations. This is just one of many references, dating back thousands of years, to the side effects of plant-derived substances used for medical and nonmedical purposes. Not surprisingly, there have been several points in history where the public's interest in such substances waned as harmful—sometimes lethal—effects of a drug were brought to light through its widespread use.

Yet it was not until this century that scientific scrutiny was dedicated to thoroughly investigating the effects substances of abuse have on individuals and societies. The National Institute on Drug Abuse (NIDA) supports and conducts about 88 percent of all scientific research on drug use in the United States. NIDA brings to NIH more than 400 staff and a 1993 budget of nearly $406 million. Established in 1974, it is the largest organization devoted to drug abuse research in the world, and has greatly contributed to

Investigators in the Neuroimaging and Drug Action Section of NIDA's Addiction Research Center are using noninvasive imaging technique to study brain structure and function in substance abusers. Here, an MRI Scan is being co-registered with a PET scan to define anatomical regions in a functional (PET) image of brain.

Sharing HIV-contaminated needles among intravenous drug users is a leading cause of the spread of AIDS. NIDA is developing strategies to encourage drug treatment as a way to control IV drug use and other addiction-related behaviors that expose drug users, their sexual partners, and their children to this deadly infection.

improved strategies for preventing illicit drug use, intervening with individuals to end their drug use, and individualizing drug abuse treatment.

Substances of abuse include heroin and other opiates, cocaine and other stimulants, sedatives, hallucinogens, and marijuana and other cannabinoids. In general, their use tends to decline as negative physiological, psychological, behavioral, and sociological effects become apparent, but many of these drugs retain their hold on individuals and societies.

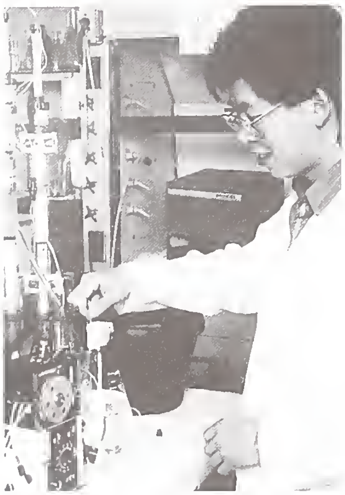
Opium, for example, had been used for centuries in China, but nearly devastated the country after a smokable form of the drug was introduced in the 1600s, resulting in an easy method of repetitive use, widespread dependence, and serious health problems. Tobacco was initially prized for its stimulant as well as calming effects, but nicotine's highly addicting effects quickly became apparent to Europeans and Japanese during the 1600s. Morphine was widely used as a painkiller during the U.S. Civil War—and cocaine was later introduced as a "treatment" for veterans who had become addicted to morphine. The abuse of amphetamines, originally an asthma treatment, was widespread during World War II; LSD, a drug once used in psychotherapy, became popular in the 1960s; in the 1970s, the media frequently publicized the negative effects of PCP, which had originally been studied as a possible anesthetic; and in the 1980s, the emergence of a smokable form of cocaine—crack—resulted in the same sort of destructive impact on modern culture that smoked opium had caused for nearly 200 years in China, putting to rest the myth that cocaine was not addictive.

PREVENTING DRUG ABUSE

One of NIDA's major goals is to prevent drug abuse before it starts by elucidating the harmful effects and addictive potential of drugs prior to their availability through prescriptions or illicit channels. By conducting and supporting research to determine the abuse liability and harmful effects of substances before they are used, NIDA provides the scientific base from which education, prevention, and treatment programs can be designed to help individuals avoid drug dependence and damage to their lives.

Since its official establishment as an institute in 1974, NIDA has pioneered all areas of the research continuum, investigating how drug use may alter

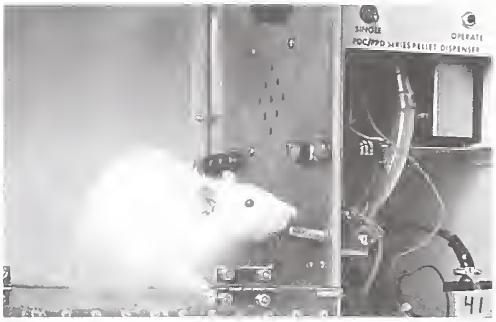
> *"NIDA is unique in the breadth, scope, and diversity of the research enterprise we support, from the molecular to the individual level."*
>
> *—Richard A. Millstein, NIDA's acting director.*



A researcher at NIDA's Addiction Research Center isolates and purifies cocaine receptors, which will be used to help scientists investigate the biological basis of cocaine addition.

physiology, behavior, the quality of life and relationships, even our national economy. "NIDA is unique in the breadth, scope, and diversity of the research enterprise we support, from the molecular to the individual level," observes Richard A. Millstein, NIDA's acting director. "Our research program encompasses contributions from epidemiological, basic biomedical and neurobehavioral, clinical and applied studies, increasing our understanding of the complex and interactive processes that underlie not only drug abuse and dependence, but also the link between research findings and their application as effective drug abuse prevention and treatment technologies."

NIDA's intramural research facility— one of the oldest organizational units in the Public Health Service—has been one of the world's primary sources of scientific knowledge on drug dependence. The Addiction Research Center (ARC), now located on the campus of the Francis Scott Key Medical Center in Baltimore, MD was established in 1935 for narcotic research at the PHS Hospital in Lexington, KY. Under NIDA, the ARC enhances research in the extramural program by carrying out multidisciplinary research on the causes, hazards, treatment, and prevention of drug abuse and addiction; the nature of the addictive process; and the abuse liability of new drugs. The center also serves as a major training resource for researchers in the field of drug abuse.



NIDA-funded scientists investigating the underlying mechanisms of compulsive drug use in humans have developed an animal model of drug abuse. By pressing the lever, the rat is able to voluntarily self-administer drugs. Drugs that animals repeatedly self-administer are generally the same drugs to which people become addicted.

STUDYING THE BRAIN AND BEHAVIOR

Studies of the brain and behavior are high priorities in NIDA's extramural and intramural programs. To fully understand drug abuse, one must understand how drugs initiate the chemical reactions in the brain that ultimately produce compulsive drugseeking behavior. In addition, scientists must clarify how environmental variables interact with brain chemistry to modulate an individual's vulnerability to addiction and drug-using behavior.

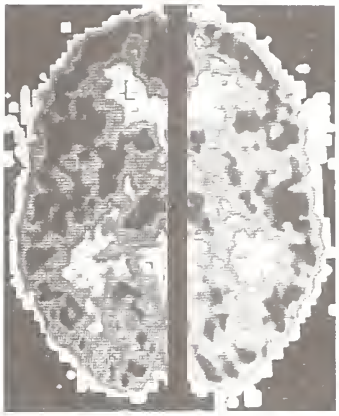
NIDA-supported neuroscience research led to the discovery in the mid 1970's of opiate receptors and endogenous opioids—which revolutionized thinking not only about the biological mechanisms underlying the addictive process, but about brain function in general. The concept of drug/receptor interactions provided the first clue about how drugs exert their effects on the brain. The receptor discovery has had widespread implications for biomedical research in a variety of scientific fields. The recognition of many nonopiate receptors and neurotransmitters, for example, was stimulated by the previous work on narcotic receptors.

More recently, in October 1991, scientists at ARC and Johns Hopkins University School of Medicine announced that they had successfully cloned the gene for the rat brain protein on which cocaine acts to produce its euphoric and addictive effects—a finding that has important implications for the treatment of cocaine addiction. According to Dr. George Uhl, chief of ARC's Molecular Neurobiology Laboratory, "For the first time, we can understand the molecular mechanism by which cocaine works. We can now try to dissect regions of the protein necessary for cocaine binding, separate them from those that transport dopamine, and speed development of drugs to block cocaine action but leave dopamine uptake intact." This should hasten the development of medication for blocking the acute effects of cocaine and perhaps for reducing cocaine craving.

RESEARCH ON TREATMENT

Much NIDA-supported research has been directed to improving treatment approaches, as the spread of HIV/AIDS through injection drug abuse, and the high-risk sexual behavior associated with drug abuse in general, have heightened the need for more effective therapies. With treatment options designed to help individuals overcome the physically toxic effects of drugs as well as the environmental and behavioral challenges, many individuals are overcoming drug addiction and improving not only their own lives, but also the quality of life for their families and communities.

A major focus of NIDA's treatment research program has been developing new medications to restore a degree of normalcy to brain function and behavior so that other therapies and rehabilitative measures, such as counseling and psychotherapy, can be more effective. NIDA has identified about 20 compounds that are potentially useful as drug treatment medications. LAAM, a treatment for heroin addiction, and buprenorphine, also a heroin addiction treatment that appears to be effective against cocaine as well, are now undergoing clinical trials. More than 400 patients at 23 sites have been treated with LAAM, and more than 450 at 12 sites with buprenorphine. A New Drug Application (NDA) is expected to be approved soon for LAAM, bringing on line for use in clinical practice an opiate agonist that offers an alternative to methadone. An NDA for buprenorphine is expected to be filed in fall 1994.



Positron emission tomography (PET) is an excellent tool for observing how drugs alter the functioning of the human brain. These images, produced by a PET scanner, show the same person's brain activity before, left, and after an injection of morphine. Lighter shades of gray indicate decreased brain activity.

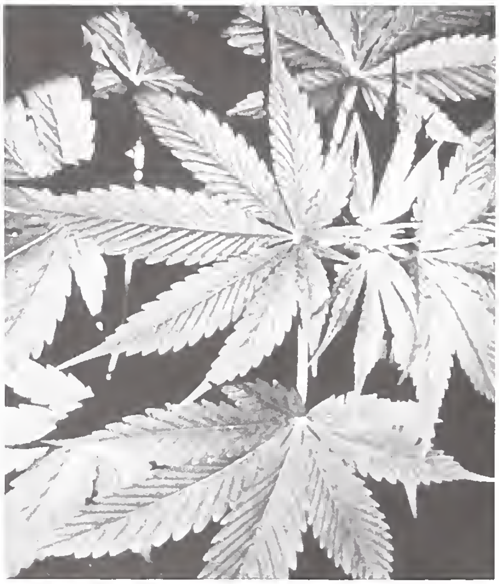
AIDS AND DRUG USE

The spread of HIV infection and AIDS has had a significant effect on

NIDA's research program. About a third of the U.S. AIDS cases can be attributed to involvement with drug use directly, or indirectly through sexual contact with a drug user. In September 1990, NIDA initiated the Cooperative Agreement for the AIDS Community-Based Outreach/Intervention Research Program. There are now 17 sites in this program; a number of additional meritorious applications are being considered. Through the program's outreach interventions, NIDA is reaching a high-risk population for HIV/AIDS that has never been in drug abuse treatment. Of those individuals contacted, 44 percent have never been in treatment, and 35 percent have never had HIV antibody testing. Others have been in treatment and are currently chronic heavy drug users. The NIDA standard intervention includes street-based outreach prevention, risk reduction activities, and HIV pre- and post-test counseling—with 80 percent of those tested returning for their results. To date, about 13 percent of the recruited population have tested HIV seropositive. These figures support the rationale for continued efforts to reach and recruit out-of-treatment drug users.

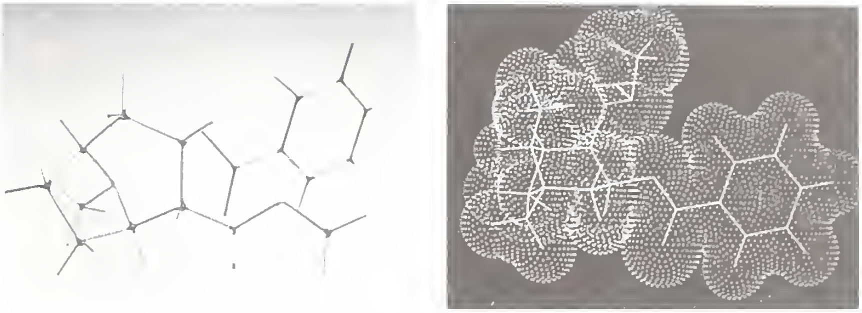
FACTORS THAT INFLUENCE DRUG USE

NIDA's research into factors that make individuals vulnerable to drug use has identified many new areas that the institute is now exploring. While human studies of adopted siblings have shown it is doubtful that a single drug abuse "addiction gene" exists, it



Marijuana remains the most commonly used illicit drug in the United States—more than 66 million Americans have used the drug at least once in their lives.

Coca leaf, cocaine powder, and crystals of crack. NIDA's most recent National Household Survey on Drug Abuse indicates that an estimated 662,000 Americans used cocaine, or its smokable derivative known as crack, once a week or more in 1990.



Advances in technological capabilities have greatly aided NIDA in studying drugs. For example, the computer-generated model of a cocaine molecule (right) provides a more detailed picture of cocaine's structure than was possible with earlier models (left).

appears that vulnerability may result from interaction among several genes. NIDA's scientists at the ARC have developed a genetically altered strain of mice for use in studying which genetic factors influence drug abuse. NIDA also is conducting long-term studies on comorbidity, to gain a better understanding of the relationship between drug abuse and psychiatric disorders, and to develop ways to diagnose individuals with both psychiatric and drug abuse problems.

In addition, NIDA has established a Vulnerability Research Center, addressing such topics as how environment, culture, and family factors predispose an individual to drug use. Research here is conducted through a consortium with the University of Pittsburgh School of Medicine and the St. Francis Medical Center in Pittsburgh. The central project is a 20-year longitudinal study of children of identified substance abusers. All of the data are being consolidated into an integrated database to examine interrelationships and determine what causes some vulnerable children to develop a drug abuse problem. The study also could help identify factors that protect vulnerable children from becoming drug abusers.

SUPPORTING NATIONWIDE ANTI-DRUG EFFORTS

Under NIDA's auspices, research on the epidemiology of illicit drug abuse and its consequences has served as the foundation upon which the nation's anti-drug efforts have been built. For example, NIDA's "Monitoring the Future" study, also known as the National High School Senior Survey, has tracked drug use among high school seniors and graduates since 1975. Responses to this study have revealed vital information about current drug abuse trends and practices among a group poised to enter college, the workforce, or the military. It is considered a valuable indicator of drug use trends because its methodology has been consistent over time.

On a more regional scale, NIDA's Washington, D.C. Metropolitan Area Drug Study (DC-MADS), a 3-year study begun in 1990, is providing a comprehensive analysis of illicit drug use in the Washington, D.C. area. It is collecting information on groups that are usually missed by surveys such as the homeless, transients, the chronically mentally ill, institutionalized individuals, and high school dropouts. This study has another function as well—it is expected to serve as a model for future studies on hard-to-reach and hidden populations.

An important adjunct of NIDA's

research is the dissemination of findings to researchers, practitioners, and the general public. NIDA researchers and grantees regularly present their findings and work-in-progress at national and international scientific forums and publish their results in numerous professional journals. Findings are also conveyed through a variety of publications, including a monograph series; *NIDA Notes,* the institute's newsletter to the field; and *NIDA Capsules,* which abstract timely and important information for scientists, practitioners, and the public. NIDA's public education campaigns cover a wide range of activities designed to educate the public about drug abuse. For additional information, contact Susan David, chief of NIDA's Community and Professional Education Branch at 301-442-1124. ▲

—*Sheryl Massaro, public affairs specialist, NIDA.*

Alcohol Research at NIH: From Cell to Society

In 1791, the College of Physicians of Philadelphia petitioned the newly formed U.S. Congress to take action against alcoholism. Comparing the disease to a plague, the physicians asked whether any government faced with alcohol-associated health and social problems could fail to take major action.

Major action in modern times centers in the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the nation's lead institute for research on the causes, consequences, prevention, and treatment of alcohol abuse and alcoholism. NIAAA joined NIH last October, with almost 300 intramural and extramural program staff and a budget of $184 million for 1992.

Genetic researchers study familial transmission of vulnerability for alcoholism.

NIAAA's extramural program currently supports more than 400 awards to researchers in medical centers and universities across the country. The Institute also administers 14 diverse Alcohol Research Centers that focus on specific areas of alcohol study, including developmental effects of alcohol on adolescents, alcohol and the cell, alcoholism treatment, and alcohol abuse prevention. In addition, scientists in six intramural laboratories conduct investigations in priority areas of the alcohol research agenda.

ALCOHOLISM AS A PUBLIC HEALTH PROBLEM

Created in 1970 at the urging of persons whose lives had been affected directly by alcoholism, NIAAA first was charged with addressing the severe public health need for alcoholism treatment. The Institute's first decade was devoted largely to eliminating barriers to care and to reducing stigma through a variety of education and information campaigns focusing on alcoholism as a disease rather than a criminal justice or mental health issue.

Only during the past decade has the Institute's primary mandate been research, research training, and research dissemination.

According to Dr. Enoch Gordis, Director since 1985, NIAAA's evolution as a research institute is essential to the general alcohol field and to practitioners in related health care areas. "Until we answer such basic questions as the central and elusive question about alcoholism—why a pathological appetite for alcohol exists at all—optimal prevention and treatment strategies also will remain elusive," he said.

Gordis views the recent NIH merger as a culmination of NIAAA's research mandate. "We now have a clear opportunity to solidify the position of alcohol research in the mainstream of biomedical and behavioral research and, simultaneously, to expand our longstanding interest in linking the two."

Two hundred years after the Philadelphia physicians identified a "plague" of alcohol problems in colonial America, almost 10 percent of adult Americans still meet standard diagnostic criteria for alcohol abuse or alcoholism. Approximately 25 percent of persons admitted to urban hospital beds screen positively for alcohol-related conditions.

Alcohol affects almost every organ system and alcohol abuse affects every aspect of society. Alcohol-related medical effects include liver disease, pancreatitis, cardiovascular disorders, and brain damage that can range from mild neurobehavioral deficits to profound dementia. Alcohol was involved in approximately 107,800 deaths in 1988, of which almost 19,000 (such as alcoholic liver cirrhosis) were directly attributable to alcohol. In addition, alcohol abuse and alcoholism in the United States impose economic costs estimated at $98.6 billion each year.

NIAAA SEEKS ANSWERS TO ALCOHOL PROBLEM

Since 1981, NIAAA's primary mission has been to generate new knowledge to confront the human and economic costs of alcohol abuse and alcoholism. Because alcoholism is a complex disease with genetic and environmental factors, the NIAAA has a multidisciplinary research program that includes behavioral as well as biomedical research. NIAAA seeks answers to essential questions including why people drink at all; why some people are vulnerable to dependence or alcohol-related disease and others are not; the relationship of genetic and environmental factors in risk for alcoholism; the mechanisms whereby alcohol produces its effects, including

> *"We now have a clear opportunity to solidify the position of alcohol research in the mainstream of biomedical and behavioral research and, simultaneously, to expand our longstanding interest in linking the two."*
>
> *—Dr. Enoch Gordis, NIAAA Director.*

organ damage; how harmful drinking and related problems can be prevented; how drinking behavior can be modified (that is, how treatment can be improved); and how to alleviate the massive economic costs of alcohol problems.

Two multisite, multidisciplinary collaborative studies exemplify the type of research required to provide answers to these questions. To identify the genes that confer susceptibility to alcoholism, scientists at six universities in the Cooperative Agreement on Genetics of Alcoholism are conducting detailed diagnostic testing and genetic typing of 2,400 persons in several hundred families in which alcoholism may be inherited. This project will define various types of alcoholism and the contribution to each of genetic and environmental factors, enable preventive interventions with high-risk individuals, and lead to the development of new treatments.

In another major study, NIAAA's landmark collaborative trial of patient-treatment matching seeks to determine the most effective interventions for various types of patients by matching 1600 alcoholism patients to three separate treatment models. Results from this first national matching study, under way at nine sites, are anticipated to improve alcoholism treatment effectiveness and cost-effectiveness.

NIAAA'S INTRAMURAL PROGRAM

The NIH campus-based Division of Intramural Clinical and Biological Research similarly has exemplified NIAAA's bench-to-bedside approach since 1983, when the institute opened an outpatient unit at NIH. One year later, the NIH Clinical Center began to admit patients for alcoholism treatment and research. The combination of well-equipped research laboratories and clinical units offers NIAAA's intramural scientists the opportunity to formulate hypotheses in laboratory and clinical settings and to test those hypotheses in readily available clinical populations.

Senior investigators in the intramural program are internationally recognized scientists in basic and clinical electrophysiology, brain imaging, molecular genetics, developmental and behavioral pharmacology, intermediary metabolism, and cell membrane functioning.

According to Dr. Markku Linnoila, Scientific Director of the Division of Intramural Clinical and Biological Research, "The recent reorganization formalizes NIAAA's longstanding relationship with other NIH institutes and facilitates scientific exchange—both among NIAAA components and throughout the NIH community."

Other research areas include: studying genetic predisposition to alcoholism, developing approaches to lessen the effects of maternal drinking on the fetus, brain imaging studies to characterize the nature of alcoholism and associated disease features, and identifying new medications for arresting or alleviating alcoholism.

Medications development is among

the most active areas of NIAAA research. Two research teams recently reported success in reducing craving and preventing relapse in treated alcoholics using the opioid antagonist naltrexone. In addition, NIAAA researchers are testing other medications for preventing relapse, as well as medications for treating alcohol-related pathologies, managing acute withdrawal, arresting intoxication, and treating alcohol-induced cognitive impairment. The successful identification of medications begins a new era in which pharmacological agents combine with traditional behavioral and verbal interventions to vastly improve alcoholism treatment outcome.

NIAAA disseminates results from its research program in a variety of publications, including the quarterly scientific journal *Alcohol Health & Research World,* the quarterly bulletin *Alcohol Alert,* monographs, and special reports. ETOH, a bibliographic data base of more than 80,000 records from scientific journals, monographs, and conference papers, and other sources, and the Quick Facts electronic bulletin board of epidemiologic information are available to investigators and others. For additional information, contact NIAAA's Office of Scientific Affairs, 301/443-3860. ▲

—Ann Bradley, press officer, NIAAA.

Experts Report Improved Approaches for Osteogenesis Imperfecta

> *"Although there is no cure for OI, the disease can be managed."*

From the time he was 8 years old until he turned 24, Paul Hearne lived in a full body cast extending from mid-chest down the length of both legs, which were separated by a bar. The cast was changed once a year. Before that, beginning at age 4, he was in more that he was out of traction. The cycle was continuous and vicious: he would get out of traction after his broken right leg had healed, only to be put back in the next day to allow his newly broken left leg time to mend.

Hearne, who is now 43, married, an attorney, and the president of the Dole Foundation in Washington, D.C., has suffered hundreds of fractions of the femur, which is the bone extending from the hip to the knee. Hearne has osteogenesis imperfecta.

Osteogenesis imperfecta (OI), also known as brittle bone disease, is a genetic disorder affecting the body's connective tissue. OI results from a defect in one of the genes that codes for type I collagen, the major structural protein of bone and skin. It is characterized by extremely fragile bones that are highly susceptible to fracture from even mild forms of trauma. For example, one 34-year-old woman with OI was simply walking down a sidewalk when she stubbed her toe and suffered a fracture of the femur.

Other characteristics of OI include short stature, which was once thought to be the result of repeated fractures, but is now attributed to a defective bone matrix; scoliosis (curvature of the spine); bowed legs; heart abnormalities; hearing loss; and dislocated joints. People with OI may also have discoloration of the sclerae (the normally white area of the eye surrounding the cornea), and may be prone to bruising and excessive sweating. Prevalence of the disease is estimated at from 1 in 20,000 to 1 in 30,000 people.

At a recent conference of scientific experts in the field of OI research and treatment, Hearne told of his experiences growing up with OI. A joint effort by the National Center for Medical Rehabilitation Research of the National Institute of Child Health and Human Development (NICHD) and the National Institute of Arthritis and Musculoskeletal Diseases and the NIH Clinical Center, the conference addressed the pathology and etiology of the disease, mouse models used for genetic research, and surgical management of OI patients. The conference was organized by Dr. Danuta Krotoski of the NICHD's National Center for Rehabilitation Research, and was co-chaired by Dr. Lynn Gerber of the Clinical Center, Dr. Peter Byers of the University of Washington, and Dr. Joan Masini of the NICHD.

OI, which may range from mild to severe, is classified into four types. Type I, the least severe, is characterized by mild to moderate fragility of the bones;

deformity is absent. Dentinogenesis imperfecta (DI), a condition in which defective formation of the dentin causes the teeth to appear brown, is present in some, but not all, people with type I.

Type II is the most severe form of the disease; it usually results in perinatal death, although proper treatment and care may enable these patients to survive for several months to a few years. People with type III have severe bone fragility, usually suffering fractures *in utero,* severe osteoporosis, extreme short stature (virtually 100 percent of patients with type III have short stature), and scoliosis. They may also have macrocephaly (head enlargement) and a triangular-shaped face. Fractured bones in these patients usually become bowed with healing, resulting in deformity.

Type IV patients have bone fragility, bowing, and osteoporosis; they may or may not have moderate short stature and DI. Barring brain injury, mental development in all four types is normal. "My impression is that children with OI are similar to other children in many ways," said Dr. Lawrence Charnas, head of neurogenetics in NICHD's Human Genetics Branch.

Although there is no cure for OI, the disease can be managed. In the days when Hearne was growing up, immobility was thought to prevent fractures; hence, the widespread use of plaster casts like the one in which he spent his youth. Today, however, immobility is actually thought to cause fractures by weakening the bones through disuse.

The current method of treatment involves a surgical intervention known as "rodding." In this procedure, a stainless steel rod is inserted as an internal splint to straighten the bone. The treatment reduces the incidence of fractures by ameliorating the bone deformity, which often is the underlying cause of fracture. In addition, rodding may help prevent deformity from progressing. The rods last about 6 years, which means that young children need repeated surgery.

While rod insertion is an effective form of treatment for some patients, it is not foolproof. Problems associated with the rods include their failure to elongate as the child's bones grow; migration out of the proper position; bending; and fractures that occur beyond the length of the rod. "The rod, no matter how good, is going to fail if the bone doesn't take over and handle the stress," said Dr. Michael Reing of Virginia Children's Hospital in Fairfax, VA. Infections may also be a complication, although they occur in only a small number of patients.

In the past, the flip side of the emphasis on immobility was on walking. Some parents of children with OI felt that walking must be achieved—through surgery, if necessary—if their children were to lead normal lives. Many surgeons tended to view walking as the ultimate goal as well, overlooking the long-term care of these patients, noted Dr. William Cole, professor in the department of orthopedics at Royal Children's Hospital in Australia.

Today, however, walking is no longer viewed as the only means of mobility available to children with OI; rather mobility in general is emphasized. An electric wheelchair could be provided at an early age, and surgery and walking could perhaps come later, Cole said. "I think we've improved our overall approach to the problem," he added.

Part of this improvement is due to a more individualized approach to treatment. Hearne, a world traveler who is in a wheelchair, emphasized that physicians must not treat OI patients in a vacuum, but within the context of their unique lives, abilities, and desires. "Part of my effort was that I was constantly expanding my environment," Hearne explained. "I expanded it from the front room of the house to the kitchen, from the kitchen to the school, from the school to the university, from the university to the country, and finally from the country to the world." ▲

—Anne Blank, writer/editor, NICHD.

Gene For One Type of Hereditary Deafness and Blindness is Identified

The first crucial step in identifying the cause of one type of hereditary deafness and blindness has recently been reported by scientists who have mapped a gene responsible for the disorder Usher syndrome (US) type I. This work was funded in part by the National Institute on Deafness and Other Communication Disorders (NIDCD).

US type I, a hereditary disorder characterized by severe hearing loss, late-onset blindness due to retinitis pigmentosa, and complete loss of balance, affects approximately one of every 18,000 people. It is an autosomal recessive disorder, which means that the responsible gene from both parents needs to be transmitted for a child to inherit the syndrome. Parents who carry the gene have a 25 percent chance of passing the disorder on to their child.

"The mapping of this gene brings scientists closer to finding an effective method for the prevention and treatment of this syndrome," said Dr. James B. Snow, Jr., NIDCD director.

Studies which enabled scientists to map the US type I gene were led by Dr. William J. Kimberling from the Center for Hereditary Communication Disorders at the Boys Town National Research Hospital, Omaha, Nebraska. Dr. Kimberling's research was partially funded by the NIDCD. Other team members include scientists from around the world, including Dr. Richard J.H. Smith from the Molecular Otolaryngology Research Laboratories at the University of Iowa, a member of an NIDCD-supported international consortium of scientists committed to locating and characterizing the genes responsible for US. Their report appeared in a recent issue of the medical journal *Genomics*.

To map the gene, Dr. Kimberling's team analyzed the hereditary material extracted from blood samples of 48 affected individuals from 27 families. Unaffected family members, including all children, both parents and available grandparents, also were tested. The families in this study were from the United States, Sweden, Ireland, and South Africa.

Gene mapping is a process where scientists determine the relative location of a specific gene on one of the 23 pairs of chromosomes found in each cell of the body. Scientists then attempt to copy or clone the gene in the laboratory to decode the gene, or to identify a gene defect. Once a gene defect is identified, scientists hope to be able to study new forms of treatment.

A factor complicating the study of US is that there are several subtypes of the disorder. According to Dr. Kimberling, scientists agree on the existence of two subtypes referred to as US type I and US type II. He added that there are possibly two other subtypes of US; however, there is no universal agree-

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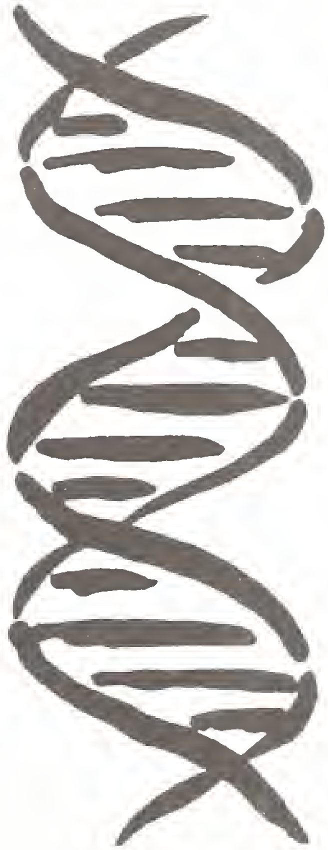

ment on the number and definition of additional subtypes.

Scientists differentiate US types I and II by the degree of hearing impairment and the presence or absence of balance problems. US type I patients have severe hearing loss, complete loss of balance and blindness; US type II individuals are affected by moderate hearing loss and blindness. Together they account for approximately 10 percent of all hereditary deafness.

Dr. Kimberling reports that current evidence suggests at least five possible genes responsible for the two types of US. While his group mapped a gene for US type I to the long arm of chromosome 11, a team led by Dr. Smith from the Usher consortium reports mapping a gene for US type I to the short arm of chromosome 11. The location of another gene for US type I has been mapped to the long arm of chromosome 14. Although a US type II gene has been mapped to the long arm of chromosome 1, the gene for five percent of US type II families cannot be mapped to that location, suggesting the existence of another gene.

The diverse clinical and genetic picture of Usher syndrome adds to the importance of this recent discovery. Dr. Kimberling, who has been studying this disorder since 1984, will continue his investigations of both Usher types I and II with the ultimate goal of finding an effective method for treating and/or preventing this syndrome.

The NIDCD supports and conducts research on normal and disordered mechanisms of hearing, balance, smell, taste, voice, speech and language. ▲
—Jo Bagley, technical writer/editor, NIDCD.

Patients' Own Immune Cells Used in Experimental HIV Therapy

An innovative pilot study sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) is evaluating the treatment of HIV-infected persons with large numbers of their own HIV-fighting immune cells grown in the laboratory. HIV is the virus that causes AIDS.

The study will assess the safety and feasibility of infusing HIV-infected persons with cytotoxic "killer" T cells that have been taken from their blood, selected for their ability to kill HIV-infected cells and cultured in the laboratory.

"Cytotoxic T cells, sometimes called killer T cells, are important weapons in the body's immune defense against viruses, including HIV, that have infected cells," explains Dr. Anthony S. Fauci, NIAID director. "Previous studies suggest that patients who progress to the late stages of HIV infection may lack functional cytotoxic T cells."

Between 15 and 24 patients will take part in the study at the New England Medical Center in Boston, a site of the Division of AIDS Treatment Research Initiative (DATRI), one of NIAID's three AIDS clinical trials networks. Study physicians will enroll patients with CD4+ T cell counts in the range of 100 to 400 per cubic millimeter of blood. CD4+ T cells are the crucial immune system cells depleted during HIV infection. Patients in the study will continue to take any prescribed anti-HIV medications and preventive drugs for *Pnemocystis carinii* pneumonia, a common HIV-related lung infection.

After physicians evaluate the participants' health with physical examinations and laboratory tests, the investigators will test blood samples from eligible patients to determine whether their cytotoxic T cells can kill HIV-infected cells. Selected cells will

The human immunodeficiency virus, which causes AIDS.

then be grown in the quantities required for infusion. At a subsequent visit to the hospital, patients will be admitted for the night and receive intravenous transfusions of 1 billion, 5 billion or 25 billion cytotoxic T cells derived from their own blood. Study investigators will follow the patients for 24 weeks to determine the effects of the treatment on their infections and to monitor any side effects.

"This is a highly complex and labor-intensive study, said Dr. Daniel F. Hoth, director of NIAID's Division of AIDS. "As a result, it likely will not be possible to infuse more than one patient per month. Two years may be required to complete the study, but this study design should provide us with the most definitive data to use to assess this therapy."

In previous laboratory studies, the blood from approximately two-thirds of HIV-infected patients has shown the ability to kill HIV-infected cells. The investigators anticipate screening 40 to 64 patients to attain the desired number of study participants.

"Innovative approaches to treatment, such as this latest DATRI study, are crucial to our goal of making HIV a manageable disease," said Hoth. "Currently only AZT, ddI and ddC in combination with AZT have been approved for treating HIV infection. These therapies can slow the progression of HIV disease but have not been shown to control it." ▲

—Greg Folkers, technical writer/editor, NIAID

Gender, Lifestyle, and Colorectal Cancer: Unanswered Questions and Opportunities for Future Research

Colorectal cancer is the second most frequent cancer among American women and the third leading cause of all cancer deaths. This disease may take on added significance as baby boomers age and as researchers begin to answer questions about how lifestyle and gender differences may influence its development.

In the 1960s, epidemiological studies showed that colorectal cancer rates were higher among women than men, apart from risk due to age, while the reverse is true today. It was found, too, that women with breast cancer are at increased risk for colorectal cancer as are women with endometrial and ovarian cancers. These observations suggested that reproductive and hormonal factors might affect colorectal cancer risk and prompted a number of studies, which resulted in conflicting findings.

"Many of those early studies, and even some that have been conducted fairly recently, didn't look at the effects of reproductive factors on different age groups," says Judith Jacobson, a researcher in cancer epidemiology supported by the National Cancer Institute at Columbia University's School of Public Health. Jacobson, under the direction of Dr. Alfred Neugut, is studying hormonal and reproductive risk factors for colorectal cancer and how they interact with lifestyle.

"Some of the conflicting results have come from studies on parity (having a pregnancy that results in a live birth). For instance, parity has been shown to increase the risk for breast cancer in women under 50, but, in older women, it appears protective. Colorectal cancer may have a similar pattern." Whether the shift in risk reflects menopause or age itself is not known.

Risk factors for both genders include a family history of colorectal cancer, an urban lifestyle, eating a diet high in fat and low in fiber, and advancing age. Of the 152,000 people who develop colorectal cancer each year, a little more than half are men. Of the 75,000 American women who will be diagnosed with colorectal cancer this year, the overwhelming majority will be over 60. In fact, women generally develop colorectal cancer a few years later than men. In younger men and women, the disease appears to have a stronger genetic component. Colorectal cancer takes the lives of approximately 57,000 people each year.

As in women, certain reproductive factors have been found to be protective in men. The few studies that have considered these issues in men have shown that having children and being married may decrease the risk for colorectal cancer. "However, what we're

> *"However, what we're seeing in these studies may be an effect of overall lifestyle rather than specific hormonal influences."*
>
> *—Judith Jacobson, Columbia University's School of Public Health.*

seeing in these studies may be an effect of overall lifestyle rather than specific hormonal influences," says Jacobson. "Marital status may reflect underlying good health or other factors such as a healthier diet and lifestyle, which may go along with being married," she explains.

DIETARY FACTORS

Researchers have been particularly interested in studying the role of diet in colorectal cancer. Several studies in men and women have shown that a diet high in saturated fat and low in fiber increases the risk of adenomatous colon polyps— precursors of colon cancer. In a recent related study, Dr. Neugut with Gail Garbowski and others at Columbia University and the Mount Sinai Medical Center in New York City, interviewed almost 2,000 patients with either first-time or recurrent polyps to determine the role of diet. They found that only among the women was there an increased risk associated with a high-fat, low-fiber diet in both initial and recurrent polyps. Acknowledging that the results are puzzling, the researchers add that a previous study, a randomized intervention trial, also showed an association between diet and polyps for women, but not for men.

"We're not sure why diet didn't seem to be as important in the men in our study. It could be an anomaly or it could suggest a difference between the genders," Dr. Neugut explains. The researchers point out that the women in the study simply may have had better recall of their diet than the men.

In an earlier study, the same investigators found that a higher body mass index ,obesity, was also a risk factor for colorectal polyps in women but less so in men. Since fat cells are the main source of estrogen in postmenopausal women—the age when women are more likely to be diagnosed with colorectal cancer—obesity in women may, at least in part, increase risk for colorectal cancer by altering the body's hormone levels.

Some dietary differences do seem to explain, at least partially, why more men than women develop polyps and colorectal cancer. Women generally consume fewer calories than men and according to a recent USDA food survey, women also consume slightly less fat than men and slightly more fruits and vegetables.

Several large studies which are either under way or in the planning stages will attempt to define more clearly the dietary factors involved in colon cancer. The NCI is conducting the Polyp Prevention Trial in both men and women to determine whether reducing fat consumption and increasing fruit, vegetable and fiber intake will decrease the recurrence of adenomatous polyps. In addition, the NIH Women's Health Initiative is a large, multicenter trial studying the effect of a low-fat diet and calcium and vitamin D supplements in preventing colorectal cancer and other diseases in women.

OTHER RISK FACTORS

To date, studies on the use of oral contraceptives and replacement estrogens have shown weak and inconsistent effects on risk for colorectal cancer. Artificially induced menopause, by surgery or radiation, may be associated with an increased risk; some studies suggest that a late menopause may be protective. The researchers agree that additional studies are necessary, especially on the interaction between behavioral and hormonal risk factors.

In the meantime say the scientists, men and women should adopt a healthy lifestyle that includes stopping smoking, eating a low-fat diet, getting exercise and regular medical check-ups. "A healthy lifestyle has other benefits, whether or not it counteracts risk due to reproductive factors," Jacobson concludes. "When the baby boomers reach the age when colon cancer and other serious diseases are more likely to occur, a healthy lifestyle might help them break even." ▲

—Mary Sullivan, editor, ***NIH News & Features*** *magazine.*

NEWS BRIEFS

NIA Studies Alzheimer's Disease in Minority, Rural Populations

Responding to the need for increased medical research and health care for minorities, the National Institute on Aging (NIA) has established satellite clinics for its Alzheimer's Disease Centers (ADCs). While most ADCs are located at major university medical schools, the satellite clinics reach needy rural and underserved patients unable to travel to the larger medical centers.

One of the newest of the 27 satellite clinics provides assistance in diagnosing and managing Alzheimer's disease (AD) for the Cherokee nation. Located in Talequah, OK, at W.W. Hastings Indian Hospital, the clinic is affiliated with the ADC of the University of Texas Southwestern Medical Center in Dallas. The 70,000 Cherokees comprise the largest Native American group in Oklahoma, with 6,000 of them 65 years or older. It is hoped that more will be learned about AD in the Indian population, a group for whom there is no existing information.

Before the start of this program in 1990, patients of the ADC programs were predominantly Caucasian, fairly well-educated members of the middle class. The satellite centers will diversify the patient pool for clinical trials and expand information on minorities and special populations with AD. Other satellite centers have been founded to serve the Hispanic and African American populations in areas such as Harlem and Detroit, as well as rural groups in 13 states.

Satellite clinic physicians do not actually conduct research, but offer patients an opportunity to participate in research protocols, and clinical trials via the ADCs. Scientists at ADCs across the country translate research advances into improved care for current AD patients, attempting to ease debilitating symptoms such as memory loss, disorientation, and impaired thinking processes.

NIEHS Holds National Forum on K–12 Environmental Science Curriculum

The National Institute of Environmental Health Sciences (NIEHS) recently held an education forum, with 40 educators, scientists and policymakers attending, to establish an environmental health sciences curriculum for students in kindergarten through 12th grade.

The forum was coordinated by Dr. Marian Johnson-Thompson, NIEHS director of institutional development, who noted that concern about the environment as related to human health already provides a unifying experience in science education in some classrooms around the country. "Teachers who participated in the forum were especially glad to be included at the inception of this national effort," she said. "Sometimes teachers feel that they are only approached after all the decisions have been made."

Steven Boyarsky, an Einstein congressional fellow and science teacher at North Medford High School in Medford, OR, was the keynote speaker. He emphasized that the turning point in any educational effort is getting a consensus from the community about what the schools should be doing.

Working sessions were held on topics such as: how K–12 science educators perceive and define the environmental health sciences; the needs at the local, state, and national levels that must be addressed in developing programs in the environmental health sciences; models that already exist that might be useful in incorporating environmental health sciences activities into the K–12 science curriculum; and barriers to the development of K–12 science curricula geared toward the environment.

Further,the forum stressed the importance of coordinating resources available through government, the private sector, schools, and the research community, and the importance of identifying existing programs that work and using them more widely, added Johnson-Thompson.

"All children need to have their understanding of science enhanced as they advance through school," said NIEHS director Dr. Kenneth Olden. "As citizens and voters, everyone needs a good, updated grasp of the sciences."

NIAID and NHLBI Train Minorities in Asthma Research

Asthma-related hospitalizations and deaths are on the rise, particularly among young African Americans and other minorities. A critical factor in solving this growing public health problem is the need to increase the number of physicians practicing in inner cities as well as basic and clinical researchers from the minority community.

The National Institute of Allergy and Infectious Diseases (NIAID) and the National Heart, Lung, and Blood Institute (NHLBI) are joining the American Academy of Allergy and Immunology (AAAI) in a program to train minority individuals—high school, undergraduate, graduate, medical students, postdoctoral trainees, and investigators—to work in the field of asthma, allergy, and immunologic diseases.

NIAID, NHLBI, and AAAI will support postdoctoral level scientists for two years. In addition, the institutes will provide funding for research opportunities to minority high school, undergraduate, and medical students under the supervision of investigators at established laboratories. NIAID and NHLBI support researchers working in laboratories on the NIH campus in Bethesda, MD, as well as scientists at U.S. universities, medical schools, and research institutions.

In a joint statement announcing the program, NIAID director Anthony S. Fauci, M.D., and NHLBI director

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Claude Lenfant, M.D., said, "The Academy, NIAID, and NHLBI recognize the importance of heightened efforts in basic and clinical research to address the high rates of asthma morbidity and mortality among minorities. This is one of several initiatives undertaken by the NIH to address the issue of asthma, particularly as it affects minorities. We are pleased to work with the AAAI and to face another challenge in research today—the underrepresentation of minorities working in these scientific areas."

NIAID and NHLBI will supplement ongoing research grants with additional funds to support minority individuals in basic and clinical research in the fields of asthma, allergy, and immunologic diseases. The Academy may make awards to individuals in research programs not funded by NIAID or NHLBI.

Based in Milwaukee, WI., AAAI is the largest professional society representing allergists, immunologists, academicians, research scientists, and allied health professionals. It has more than 4,600 members in the United States, Canada, and 41 foreign countries. Among the goals of the Academy are to advance the scientific knowledge and public awareness of allergy and improve allergy medical practices, promote and stimulate research and the study of allergic diseases.

For application information, contact Milton Hernandez, Ph.D., director of the Office of Science Training and Manpower Development in the NIAID Division of Extramural Activities at 301-496-7291 or J. Sri Ram, Ph.D., special assistant to the director of the NHLBI Division of Lung Diseases at 301-496-0895.

Deadly Brain Disorder Linked to Chromosome 18

Scientists at the National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Mental Health (NIMH) have linked a deadly brain disorder, called Neimann-Pick Type C disease, to a small region of human chromosome 18. The findings, which were reported in a recent issue of the *Proceedings of the National Academy of Sciences*, may eventually lead to improved diagnosis and treatment for this inherited disorder and yield new insight into the metabolism of cholesterol inside the body's cells.

"These findings represent a critical step forward in identifying the faulty gene that causes Neimann-Pick Type C disease. Once that is accomplished, we will be poised to develop specific, effective treatment for this devastating disorder," said Roscoe Brady, M.D., chief of the NINDS Developmental and Metabolic Neurology Branch.

About 300 Americans have Neimann-Pick Type C disease, in which faulty metabolism of cholesterol within cells leads to abnormal cholesterol buildup in the brain, liver, and spleen. Affected children typically develop normally until school age, then begin to regress. The first symptoms of the disease can be subtle, such as declining

> *"These findings represent a critical step forward in identifying the faulty gene that causes Neimann-Pick Type C disease."*
>
> *—Dr. Roscoe Brady, chief NINDS Developmental and Metabolic Neurology Branch.*

performance in school, but as the disease progresses, brain damage worsens, causing progressive dementia and motor problems, including difficulty with walking, talking, and swallowing. Most patients die before they reach the age of 20.

"I have high hopes that identifying the disease gene for Neimann-Pick Type C will help us learn more about how cholesterol is processed inside cells of the brain and other organs," said Peter G. Pentchev, Ph.D., an NINDS biochemist who has been conducting Neimann-Pick Type C research for more than a decade. "This information, in turn, could offer vital insights into how this process goes awry not only in this disorder, but also in such common killers as heart disease and stroke."

In the current study, a collaborative team of scientists from the NINDS, NIMH, Columbia University and the Lyon-Sud School of Medicine, France analyzed DNA samples from 12 affected families and identified a small region on chromosome 18 most likely to house the recessive disease gene. "We've drastically reduced the size of the hunt for this gene. The region we've identified covers less than 3 percent of chromosome 18, and, with a little luck, we should identify the precise gene soon," Dr. Pentchev said.

"Scientists will then be ready to determine the corresponding protein defect and to devise new treatments, including drugs designed to intervene in the disease process and protein or gene replacement therapy," Dr. Brady added.

The NINDS is the nation's leading supporter of research on disorders of the brain and nervous system and a lead agency, along with the National Institute of Mental Health, for the congressionally mandated Decade of the Brain.

NIH Launches Women's Health Studies at 16 Medical Centers

The National Institutes of Health (NIH) recently announced the selection of 16 medical centers that will spearhead the Women's Health Initiative studies. This initiative is a 15-year, $625 million study that will help medical research obtain important information on women's health.

The Women's Health Initiative will involve more than 160,000 women ages 50 to 79, making it the largest prevention trial ever undertaken in this country. The study will include research on the causes and treatments of heart disease, cancer, and osteoporosis—diseases that disproportionately kill and disable women.

The 16 Vanguard Centers will test, refine, and implement the study design and operating procedures prior to enrolling women in the first stage of the study scheduled to begin this September. Twenty-nine additional centers will be awarded contracts by the middle of 1994. Preliminary results from some of the studies are expected within four to five years.

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Each center will enroll approximately 3,940 women over a three-year period for either the clinical trial or observational study. The clinical intervention trial will look at the effects of a low-fat diet, calcium and vitamin D supplements, and hormone replacement therapy on cardiovascular disease, cancer, and osteoporosis on older women. The observational study which will include a follow up of women in the intervention trial and is the largest observational study of women ever done, will provide important information on the predictors of disease. Community-based studies will look at ways to help women adopt healthy behaviors, such as maintaining good eating and exercise habits, quitting smoking, and getting regular medical exams. Together these studies will provide women and their physicians scientifically sound information about healthy behaviors and treatments. Recruitment efforts will focus on medically underserved areas and minority populations. Four of the Vanguard Centers will primarily recruit minority participants in their areas.

"In terms of medical research, women have been ignored too long", said Dr. Bernadine P. Healy, former NIH Director. "These Vanguard Centers will play a pivotal role in NIH's commitment to include women in medical research and gather vital data to help treat the unique problems that afflict women. Today we are entering a new age in women's health research."

> *"In terms of medical research, women have been ignored too long."*
>
> *—Dr. Bernadine P. Healy, former NIH Director.*

The 16 Vangard Centers announced are:

Bowman Gray School of Medicine
Winston-Salem, North Carolina

Brigham & Women's Hospital
Boston, Massachusetts

Emory University School of Medicine
Atlanta, Georgia

Fred Hutchinson Cancer Research Center
Seattle, Washington

The Memorial Hospital
Pawtucket, Rhode Island

Northwestern University Medical School
Chicago, Illinois

State University of New York
Buffalo, New York

University of Alabama
Birmingham, Alabama

University of Arizona
Tucson, Arizona

University of California
Davis, California

University of California, San Diego
La Jolla, California

University of Iowa
Iowa City, Iowa

University of Medicine and Dentistry of New Jersey
Newark, New Jersey

University of Minnesota Medical School
Minneapolis, Minnesota

University of Pittsburgh
Pittsburgh, Pennsylvania

University of Tennessee
Memphis, Tennessee

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Malnourishment in Infants Can Affect Tooth and Jaw Development

BY JAN EHRMAN AND PAT SHERIDAN

Children who suffer malnutrition early in life may experience developmental problems of their teeth and jaw, according to the results of a long-term study conducted by National Institute of Dental Research grantees.

Experts have long known of the harmful effects of childhood malnourishment on growth, development, and behavior. Recent research has now demonstrated that chronic hunger may have even broader consequences for oral health.

Dr. Jose Alvarez and his associates at the University of Alabama in Birmingham began providing dental care to a group of 209 Peruvian infants in the mid-1980s.

Although healthy and normal at birth, all of the infants became clinically malnourished before their first birthday. Even though the malnutrition was quickly reversed upon treatment, the scientists found that by age four, 37 of the youngsters who had suffered prolonged, moderate malnutrition had developed a significantly higher number of cavities within their primary (baby) teeth, compared to well-nourished children from the same community.

When the children were re-checked at age 6, Alvarez and his team discovered that the early malnutrition appeared to have stunted the growth of certain facial bones, primarily the lower jaw. An underdeveloped jaw commonly causes tooth crowding and bite problems.

In addition, these youngsters experienced an abnormal pattern of tooth development, in which the eruption of the primary teeth was delayed, but the eruption of many of the permanent teeth occurred much earlier than normal. Malnourished children whose permanent teeth had surfaced by age 6 were also more likely to have cavities than 6-year-olds who had not suffered malnutrition.

"What we discovered and what we now know with certainty is that malnourishment can promote a variety of oral health problems. And these problems may extend well past the pediatric stage into adolescence and beyond," explained Alvarez. He added, "This further adds to the cumulative body of evidence of the very real dangers of malnourishment and chronic childhood hunger, and why we must fight to prevent this dreaded problem, both in the United States and abroad." ▲

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National Institutes of Health
Department of Health and
Human Services

Alvarez reported his findings at the annual meeting of the International Association for Dental Research, March 10-14, 1993, Chicago, IL. A paper expanding on these findings will soon be published in the ***Journal of Dental Research****.*

For more information on dental care and oral health, contact the Information Office, National Institute of Dental Research, NIH, 9000 Rockville Pike, Building 31, Room 2C-35, Bethesda, MD, 20892, ph: (301) 496-4261.

Jan Ehrman is editor of ***NIH News and Features****. Pat Sheridan is a technical writer/editor with NIH's National Institute of Dental Research.*

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EDITOR
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Rodent Model Yields Access to Understanding of Bone Loss; May Give Rise to New Treatments

BY SUZANNE M. LEWIS

A team of Federal scientists has laid important groundwork that may lead to new treatments for age-related bone loss, including the most severe form, osteoporosis.

Using a sophisticated laboratory technique, investigators at the National Institute on Aging's (NIA) Gerontology Research Center (GRC) in Baltimore rapidly and thoroughly examined the entire breakdown and buildup of rat bone in just a few weeks' time.

Dr. C. Tony Liang and his colleagues from the GRC, Mayo Clinic (Rochester, MN), Albany Medical Center (NY), and Merck Sharp and Dohme Research Laboratories (West Point, PA) used old and young rats to compare changes in the expression of genes that regulate bone resorption (breakdown) and deposition (formation). Gene expression occurs when a gene is "turned on," thus enabling the gene to deliver vital instructions to a cell, such as "form new bone."

To observe these age-related changes in bone development, the scientists staged a controlled and consistent cycle of bone resorption and deposition. Using a special syringe, they removed bone marrow (soft, fatty tissue that fills the cavities of bone) from the femur (thigh) of young and old rats. This process activated new bone formation within the marrow. The newly-formed bone was then resorbed by the walls of the marrow cavity. Within 3 weeks, the cavity again filled with new marrow.

According to Liang, "Changes in bone activity with age usually occur over an extended period, making characterization of the deficits difficult to assess experimentally. This model amplifies the age-related deficits in gene activity and bone growth in experimental animals. We were able to observe this process in only 3 weeks."

> *"This model amplifies the age-related deficits in gene activity and bone growth in experimental animals."*

By understanding what occurs at cellular and molecular levels when bones resorb and form, researchers can then test therapies that inhibit bone loss or promote bone formation. This is especially important in developing treatments for people with such debilitating diseases as osteoporosis, where bone loss is not balanced by replacement of new bone. Osteoporosis affects one in four women over age 60 and is a major cause of disability, according to the NIA. In the case of hip fractures or other serious orthopedic problems, it may also lead to premature death.

Previous studies show that the production of growth hormones, as well as sex hormones (estrogen in women and testosterone in men) usually decline with advancing age. Liang and his colleagues are hopeful that this animal model will

(CONTINUED)

serve as a means of studying the influence of hormones on gene expression. It is also possible, they believe, that one of the growth factors (proteins that cause bone cells to multiply), or other not yet identified factors, might correct the deficits in aging human bone. ▲

This study was published in the November 1992 issue of ***Bone****.*

For more information on osteoporosis or other issues related to aging, contact: Information Office, National Institute on Aging, NIH, 9000 Rockville Pike, Building 31, Room 5C-27, Bethesda, MD, 20892; phone: (301) 496-1752.

Suzanne Lewis is a public affairs specialist at NIH's Gerontology Research Center, National Institute on Aging, Baltimore, MD.

NIH RESEARCH CAPSULES

Protein Supplements Help Pressure Sores Heal

Supplementing the diets of older, bedridden patients with large amounts of protein can significantly help their pressure sores heal. These findings were reported by a scientist supported by the National Institute on Aging and his colleagues.

Pressure sores, or decubitus ulcers, are painful, open sores that often affect seriously ill, long-term care or hospitalized patients. In one study, these lesions occurred in nearly one out of five individuals newly-admitted to nursing homes.

Several factors raise the likelihood for pressure sores, including immobility, urinary incontinence, skin changes that occur with advancing age, and nutritional deficiencies—all common in the nursing home setting. Long-term care patients may suffer nutritional deficiencies (malnourishment) due to illness, dental problems, or from other causes. Meanwhile, pressure sores, combined with these risk factors, place these patients at risk for skin infections, other medical complications, and sometimes even death.

Drs. Rosalind Breslow of the University of Maryland, College Park, Andrew Goldberg of the Veterans Administration Medical Center in Baltimore, MD, and their collaborators investigated the effect of protein supplementation on pressure sore healing in the trunk area in two groups of malnourished nursing home patients who received either large or modest amounts of protein.

After 8 weeks of treatment, the researchers documented the effect of the protein. Specifically, ulcers of the trunk diminished in size in correspondence with the amount of protein consumed. They found that significant healing occurred for patients with the largest pressure sores who were consuming the most protein.

The scientists conclude that preventive therapy (giving patients at risk for pressure sores supplemental protein) for malnourished individuals stricken by the troublesome ulcers could improve the quality of life for many nursing home residents, while also reducing their overall medical costs.

Editor's Note: *This therapy may not be appropriate for patients with kidney disease or declining kidney function.*

Ref: Breslow, R.A., Ph.D., R.D., et al., "The Importance of Dietary Protein in Healing Pressure Ulcers," ***Journal of the American Geriatrics Society****, Vol. 41, No. 4, pp. 357-362, April 1993.*

Nitrate-Laden Water May Raise Risk of Juvenile Diabetes

Children who drink water that contains nitrates, even relatively modest amounts, may increase their risk for developing insulin-dependent diabetes, according to an analysis conducted by National Institute of Diabetes and Digestive and Kidney Diseases grantees.

Dr. Jill N. Kostraba and her colleagues from the University of Colorado Health Sciences Center in Denver studied the link between nitrates found in community drinking water and the development of diabetes in nearly 1,300

(CONTINUED)

children living in 63 Colorado counties between 1978 and 1988. The youths were less than 18 years of age at diagnosis of juvenile diabetes, and had been placed on insulin within 2 weeks of this diagnosis.

After matching incidence rates for diabetes against the nitrate level for each county's public water system, the researchers determined that where water nitrate levels were highest, the risk of developing diabetes more than doubled (15 cases per 100,000/children/year), compared to counties where the nitrate levels were lowest (7 cases of diabetes per 100,000 children/year).

Earlier studies had demonstrated that large amounts of nitrates or related compounds may promote diabetes by producing free radicals (potential cancer-causing substances that can induce cellular damage) in the body. It is thought that free radicals may harm the insulin-producing cells of the pancreas. This research suggests that even lesser amounts of nitrates could have the same effect.

Well water frequently contains higher levels of nitrates than water obtained from public water supplies, however in this study it was not possible to acquire data on the specific source of drinking water. It was also not feasible to determine exposure to nitrates on an individual basis, a necessity before the nitrate/diabetes link can be firmly substantiated, says Kostraba.

Ref: Kostraba, J.N, MPH, Ph.D., et al., "Nitrate Levels in Community Drinking Waters and Risk of IDDM," ***Diabetes Care****, Vol. 15, No. 11, pp. 1505-1508, Nov. 1992.*

Risk Factors Identified for Penile Cancer

A history of 30 or more lifetime sexual partners and infection with the human papillomavirus (HPV) appears to augment the risk for developing penile cancer, according to a recent study. Absence of circumcision at birth, and penile tear or rash from any cause were also associated with increased risk. Cigarette smoking was an added factor.

In the study, conducted by National Cancer Institute grantee Dr. Christopher Maden and co-workers at the Fred Hutchinson Cancer Research Center in Seattle, WA, 110 men with penile cancer and 355 healthy, control males were interviewed regarding their medical and sexual histories.

Findings on the association between heightened risk for cancer of the penis and sexual activity, HPV infection, and smoking are consistent with results from earlier studies of women and genital cancer. The results are also consistent with previous evidence that lack of neonatal circumcision and complications related to poor hygiene are linked to an increased risk for penile cancer.

The disease is relatively rare, accounting for less than 1 percent of all male cancers. Nearly 400 men died from penile cancer in 1990.

Ref: Maden, C., Ph.D., et al., "History of Circumcision, Medical Conditions, and Sexual Activity and Risk of Penile Cancer," ***Journal of the National Cancer Institute****, Vol. 85, No. 1, pp. 19-24, Jan. 6, 1993.*

NIH RESEARCH CAPSULES

Antisocial Personality Disorder Boosts HIV Dangers in IV Drug Abusers

Intravenous drug abusers with antisocial personality disorder (APD)—characterized by chronic irresponsible and reckless behaviors—are far more likely to develop HIV than intravenous (IV) drug abusers not afflicted with the behavioral syndrome, researchers report.

APD is a commonly diagnosed condition among IV drug abusers, with rates observed in some studies as high as 50 percent or greater. The finding is clinically meaningful, since drug abusers with APD typically experience poorer treatment outcomes.

In this particular study, National Institute on Drug Abuse-supported scientists, led by Dr. Robert K. Brooner of the Johns Hopkins University School of Medicine in Baltimore, investigated the association between HIV infectivity and APD in a volunteer group of 272 IV drug abusers. Each subjects' HIV status was unknown prior to the study.

The investigators conducted structured interviews and carefully analyzed the data to determine each participant's psychiatric status. They established that APD more than doubled the likelihood for HIV infectivity among the drug abusers, compared to those not afflicted with APD (18 percent vs. 8 percent).

Behavioral characteristics such as a higher rate of needle-sharing activity, greater drug dependency, and more frequent drug injections were identified among those with APD. These three factors may help explain the differences in HIV prevalence rates among IV drug abusers, say the scientists.

*Ref: Brooner, R.K., Ph.D., et al., "Antisocial Personality Disorder and HIV Infection Among Intravenous Drug Abusers," **American Journal of Psychiatry**, Vol. 150, No. 1, pp. 53-58, January 1993.*

Sunscreens Offer Only Limited Protection Against Immune Alterations in Rodents

Although sunscreens efficiently guard against sunburn, they may offer only partial defense against the development of immune suppression, animal studies reveal.

Evidence indicates that certain types of skin cancer can develop when unprotected skin is exposed to long periods of ultraviolet light. While suntan lotions normally shield against the inflammation and stinging associated with sunburn, there are differing opinions as to whether they fully defend against ultraviolet radiation (UVR)-induced immune system alterations—such as those that may precede squamous and basal cell carcinoma, two common skin cancers.

National Cancer Institute grantees, Drs. Peter Wolfe, Cerrie K. Donawho, and Margaret L. Kripke, of the University of Texas Anderson Cancer Center in Houston, looked at the protective ability of three sunscreens in healthy, young, shaved mice exposed to various doses of UVR. As expected, the sunscreens guarded well against skin inflammation (sunburn), however they

(CONTINUED)

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were not as effective in protecting against immunosuppression, especially at the higher UV doses. According to the investigators, while sunscreens do provide some degree of immune system protection, the study demonstrates their capabilities are limited. It is important to recognize, say the scientists, that the absence of skin swelling and other symptoms associated with sunburn through the use of sunscreens does not mean that the lotions fully protect the immune system from damage by the sun's ultraviolet light.

Ref: Wolf, P., Ph.D., et al., "Analysis of the Protective Effect of Different Sunscreens on Ultraviolet Radiation-Induced Local and Systemic Suppression of Contact Hypersensitivity and Inflammatory Responses in Mice," **Journal of Investigative Dermatology**, *Vol. 100, No. 3, pp. 254-259, March 1993.*

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Spring 1995

SPECIAL ISSUE

Research on Minority Health

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features

Editor
Mary Sullivan

Graphic Design
The Watermark Design Office

Office of Communications
Building 31, Room 2B10
9000 Rockville Pike
Bethesda, MD 20892
(301) 496-1766

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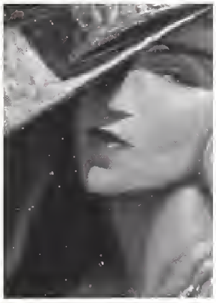

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INTRODUCTION

The increase of minorities in this country and their growing influence on our culture will profoundly affect the nation's priorities—including health—for many decades to come. Although concerns about health are universal, clearly differences exist among various groups with regard to disease and disability. Scientific research seeks to understand these differences and to develop strategies that will reduce the incidence of disease and extend the lifespan.

This is an exciting time in biomedical research. Breakthroughs in molecular biology and genetics are making it possible to identify the fundamental basis of many diseases, and offer hope for new treatments. Prevention and education play an important role in helping people maintain their health, well-being, and the quality of their lives. Minorities must share in the benefits to be gained from knowledge acquired through research as quickly and efficiently as other groups. They have carried an unequal burden with respect to disease and disability, resulting in a lower life expectancy.

> IMPROVED HEALTH FOR WOMEN AND MINORITIES IS OF MAJOR IMPORTANCE TO NIH.

The National Institutes of Health (NIH) has been a leader in minority health for several decades. In the early 1970s, the NIH supported the first centers to study sickle cell disease, a genetic blood disorder that primarily affects African Americans. But this was only the beginning. Since then every institute at the NIH has identified specific categories of disease research of significance to minority Americans. With the establishment of the Office of Research on Minority Health in 1990, institute projects on minority health were further coordinated and expanded.

In addition, NIH has been at the forefront of efforts to increase the number of minorities conducting biomedical research. Through a variety of programs, NIH supports minority students from the earliest grades through postdoctoral work. NIH recognizes that training the future generation of minority scientists is critical not only for the future of minority health research but also to ensure continued excellence in biomedical research.

As you read this special issue of *NIH News & Features*, we hope you will appreciate the successes of the past and the challenges of the future. The studies selected cover a broad range of areas from the latest research on diseases that affect minorities to public information campaigns that focus on communicating practical health information, to innovative programs designed to support minorities in scientific careers. Their common goal is to close the gap that currently exists between the health of minorities and the majority population.

We would like to acknowledge the many talented individuals who contributed to this issue. Their efforts reflect the NIH commitment to the improvement of health for all.

—Mary Sullivan, editor, ***NIH News & Features*** *magazine.*

Minority Health at NIH:

Building Partnerships for th

Dr. John Ruffin

Why was the Office of Research on Minority Health (ORMH) established at NIH and how does its mission fit into the research programs the institutes already have in place?

The office was established by the NIH Director in 1990 in response to a Congressional mandate. The House Appropriations Committee directed the NIH to develop a plan that would increase the funding and resources devoted to minority health, and to increase the numbers of minority scientists in research careers. Although the Office of Research on Minority Health was charged with the primary responsibility for accomplishing these goals, all the NIH institutes are expected to participate. ORMH's task is to strengthen and coordinate already existing programs as well as create new ones. The way ORMH has done this is by building partnerships with the Institutes, Centers, and Divisions of the NIH, as well as with other government agencies and organizations.

Which groups are considered to be minorities in this country

Traditionally, minorities have included Native Americans and Alaskan Natives, Asian Americans and Pacific Islanders, African Americans, and Hispanics. However, it is important to remember that the usefulness of minority classifications continues to change as our population becomes more diverse. In many cases we think not in terms of minorities but in terms of the underserved, a classification that includes minorities, the homeless, rural populations, and women.

What "special" health problems do minorities have?

All across the board minorities suffer from chronic and acute diseases at rates higher than whites. For example, African Americans have the highest rates of new cancer cases than any other group, and Native Americans have ten times the risk of developing diabetes as whites. African American men are almost twice as likely to die from stroke as white men. The high infant mortality rate in this country occurs almost exclusively among minority groups. The list goes on... Although obviously there are many factors contributing to the lower health status of minorities, biomedical research plays an important role in helping to reduce this disparity.

It's important to note that there is variability among minorities with regard to health problems. Not all minorities have the same rates of diabetes and hypertension, for example. A study supported by the National Heart, Lung, and Blood Institute has shown that Hispanics are less likely than whites to die of major chronic illnesses. However, they still have higher rates of illness for certain diseases, like diabetes. If we can find out why their overall death rate is lower, perhaps we can apply that information to other groups as well.

How is the NIH in general and the ORMH in particular addressing the health problems of minorities?

NIH is first and foremost a biomedical research institution, so we are mainly concerned with new scientific advances aimed at improving human health. In

Future

1985 a report from the Secretary of the Department of Health and Human Services on Black and Minority Health stated that minority Americans are not fully benefitting from the advances made in biomedical research. NIH certainly agrees with that statement, and since that report, virtually all the institutes have placed more emphasis on minority activities.

Then in 1991, the Office of Research on Minority Health appointed a Fact-Finding Team, consisting of 53 experts from universities, industry, and government, to assess NIH programs and to make recommendations for ways to increase attention given to minority health issues and to enhance the participation of minority students in biomedical careers. Three regional meetings were held where input was obtained from interested professionals and citizens regarding the status of minority health in the U.S.

As a result of these meetings, 13 recommendations were developed, eventually becoming the basis of the agenda for the Office of Research on Minority Health. A follow-up to these meetings, the National Conference on Minority Health Research and Research Training, was held last March to assist in the development of research programs in minority health for the years 1995-2000.

The cornerstone of all these efforts is the Minority Health Initiative, which aims to improve the health of minorities across the lifespan, from infant mortality to aging, and to find ways to significantly increase the participation of minorities in biomedical research.

THE FOLLOWING IS AN INTERVIEW WITH DR. JOHN RUFFIN, NIH ASSOCIATE DIRECTOR FOR RESEARCH ON MINORITY HEALTH. ON AUGUST 26, 1990, DR. RUFFIN WAS APPOINTED DIRECTOR OF THE NEWLY FORMED OFFICE OF RESEARCH ON MINORITY HEALTH (ORMH). HE DISCUSSES SOME OF THE MAJOR ISSUES IN MINORITY HEALTH AND HOW ORMH IS ADDRESSING THE HEALTH PROBLEMS FACED BY MINORITIES IN THIS COUNTRY TODAY.

WOULD YOU PLEASE DESCRIBE THE MINORITY HEALTH INITIATIVE IN MORE DETAIL?

The Minority Health Initiative, which received its first funding in 1992, is a comprehensive program involving close partnerships between the NIH institutes and the Office of Research on Minority Health to increase intramural and extramural research aimed at improving minority health. In many cases, the institutes have an already existing program in place that requires additional funding, or they may request funding for a new project. A significant number of collaborative projects involve research training as well.

One especially noteworthy project is the D.C. Minority Infant Mortality Initiative which is attempting to understand the reasons for the high infant mortality rate among minority populations in Washington, D.C. The investigators hope to develop and test interventions that will be successful in reducing infant mortality in Washington, D.C. and elsewhere. The project is being supported by the Office of Research on Minority Health in collaboration with the National Institute of Child Health and Human Development and the National Institute of Nursing Research.

Additional collaborations are focused on research to develop successful strategies to promote healthy behaviors among minority youth and to more fully understand the health problems of young adult minorities. At the other end of the lifespan, older minorities are the target of ORMH efforts in conjunction with the National Institute on Aging. Many of these projects include plans for medical and behavioral research, as well as programs for health education and community outreach activities.

The Minority Health Initiative also supports collaborative efforts with intramural scientists. Dr. Richard Klausner and colleagues at the National Institute of Child Health and Human Development are studying the high prevalence of hemochromatosis, a metabolic disease characterized by excess iron in the body, in certain African populations. The investigators are studying families with this disorder to determine the role genetic factors play in the development of this disease, which also may affect African Americans in this country. The four-year project, which began in October 1994, is under the direction of Dr. Tracey Rouault.

These are only a few examples of the wide range of programs ORMH is supporting across the board at NIH to improve minority health. To date, ORMH has collaborative projects with all the NIH institutes, the National Library of Medicine, the National Center for Human Genome Research, the National Center for Research Resources, and the Fogarty International Center.

WHAT ABOUT AIDS AND MINORITIES?

That's an important topic with many dimensions, only some of which will be addressed here. Until very recently, the impact of AIDS on minorities had been seriously underestimated. In addition to being one of the leading causes of death among young African American and Hispanic American males, much of the new HIV infection we're seeing is in women and children, many of whom are minorities.

In the early days of the epidemic, although minorities were becoming infected with HIV at an alarming rate, AIDS was thought to be largely a disease of white gay men. In part this was because minorities typically don't have the resources needed to make their concerns heard. Today there is a little more awareness of the problem, but basically minorities with AIDS remain a forgotten group with limited access to good health care, even without the complication of an AIDS diagnosis.

In terms of prevention and education, we're seeing that minorities have not always received the message about AIDS, or at least not in ways that are useful to them. Greater effort needs to be made to reach these populations.

NIH, through the National Institute of Allergy and Infectious Diseases, is conducting some interesting studies on the factors that influence minority participation in HIV clinical trials. The researchers are finding that socio-economic factors play an important role in determining whether minorities will participate and remain in clinical studies. This kind of effort will provide the knowledge needed to develop culturally and racially sensitive approaches to encouraging more minorities to participate in clinical trials.

IT'S BEEN SAID THAT IF MORE MINORITIES ENTER CAREERS IN BIOMEDICAL RESEARCH, THEN MORE RESEARCH ON MINORITY HEALTH WILL BE CONDUCTED. WHAT ARE THE NIH AND THE ORMH DOING TO SUPPORT MINORITY STUDENTS?

I think that's a fair argument to make, but certainly not the only justification for supporting more minority students interested in biomedical careers. If the U.S. is to remain economically competitive, we must find a way to attract more minority students to scientific careers. By the year 2000, 85 percent of all new participants in the nation's workforce will be minorities or women, and they represent a tremendous braintrust that must not be wasted.

The NIH has been a leader in supporting minority students since the early 1970s and our support has produced many fine minority students. However, we still have a big job ahead of us. The number of minority students in the health sciences is disproportionately low. For example, in 1990 more than 5000 doctorates were awarded in the life sciences in the U.S., but only 2.3 percent went to Hispanic Americans, 1.4 percent to African Americans, and 0.2 percent to Native Americans. These are abominable figures, especially considering the fact that these groups are becoming an ever increasing segment of our population.

Part of the problem arises from the fact that minorities are underrepresented in the sciences at every level—from elementary and secondary school science courses to the university campus. To address this situation, the NIH has developed programs that focus on recruiting and retaining minorities in the biomedical sciences all along the educational pipeline. These are ongoing programs specifically targeted toward minority researchers. They include the Minority Access to Research Careers (MARC), the Minority Biomedical Research Support Program (MBRS), the Research Centers in Minority Institutions Program (RCMI), the Research Supplements for Minority Investigators and the Minority High School Student Research Apprenticeship Program (MHSSRAP), just to mention a few. The ORMH has provided supplemental support to many of these programs.

Further, we know that a great many talented minority students are in junior or two-year community colleges, and never advance beyond that point. Our "Bridges to the Future" program is designed to assist minority students in successfully progressing to the next level of training. Two key transition points have been identified as crucial for students considering careers in biomedical research—the transition from the Associates to the Baccalaureate degree and from the Masters to the Doctoral degree. If we can support students through these transitions, they have a much greater chance at succeeding in their research careers.

NIH has several programs for minorities at the high school level as well. In June 1992, NIH signed a memorandum of understanding with the National Science Foundation to expand the life sciences components of three of its ongoing projects. Two of these projects are targeted to students at the pre-college level in order to increase the number of minorities who complete high school with sufficient preparation in the sciences to pursue further education.

Evaluation of these programs and career follow-up will ensure that our success rate continues to climb as we strive to understand the obstacles that prevent minorities from seeking careers in biomedical research and develop methods to overcome them.

IN YOUR OPINION WHAT ARE SOME OF THE MAJOR BARRIERS MINORITY STUDENTS FACE?

In addition to financial constraints which affect majority students as well, minority students, in the past, had fewer role models and faced more obstacles all along the way. Fortunately, some of this is changing. The pool of minority students is increasing and the scientific establishment is realizing that it must cultivate and nurture minority talent if scientific research is to remain a viable enterprise. NIH, through the Research Supplement Program for Underrepresented Minorities, is assisting in this effort by providing administrative supplements to NIH grantees who wish to support the research activities of minority students and scientists.

I think one approach everyone agrees on is that we must identify and attract students with potential in the very early years and not let them "fall through the cracks" of academia. This means not only providing them with financial support, but with mentors and programs that provide guidance to these young people in planning their careers.

IN ADDITION TO SUPPORTING A COMPREHENSIVE RANGE OF RESEARCH AND TRAINING PROGRAMS, WHAT ELSE IS THE NIH DOING TO CONTRIBUTE TO THE ADVANCEMENT OF MINORITY HEALTH?

Another very important effort recently undertaken by the NIH is the establishment of guidelines for including women and minorities in research involving human subjects. This effort is in response to the NIH Revitalization Act of 1993, which strengthens the existing policy.

Specifically, all NIH-supported clinical trials at Phase III, which is the final stage of testing an experimental intervention and typically involves several hundred or more participants, must include women and minorities, unless there is a compelling rationale and justification not to do so. Cost is not considered an acceptable justification for exclusion. The guidelines also call for outreach activities to be undertaken to recruit and retain women and minorities as study participants.

This policy applies to all NIH-supported research projects submitted on or after June 1994. Research funded prior to this time must comply with the former policy, which also requires an annual report on the enrollment of women and minorities. It is hoped that these guidelines will result in research that will address the significant gaps in knowledge that currently exist about the clinical differences and health problems of women and minorities.

WHAT IS THE FUTURE OF MINORITY HEALTH IN THIS COUNTRY?

The future demographics of this country will dictate that minority health will remain an important area of biomedical research. People with a mix of racial and ethnic backgrounds will increase in numbers, becoming the norm rather than the exception, and their health will become one of the nation's top priorities.

I believe the time is right for minority health in this country. We've seen progress in the last few years in terms of increased public awareness and heightened sensitivity toward this issue, but we have a long way to go. The American public can be confident that NIH will continue to lead the way in research on minority health so that all Americans can look forward to a brighter and healthier future.

Mary Sullivan, public affairs specialist and editor, ***NIH News & Features*** *magazine.*

MAJOR EFFORT STRIVES TO

Improve Health of African Americans with High Blood Pressure

RECENT DATA SHOW THAT OUTREACH EFFORTS ARE WORKING. THE PERCENTAGE OF AFRICAN AMERICANS WHO KNOW THEY HAVE HIGH BLOOD PRESSURE AND ARE CONTROLLING THEIR CONDITION HAS RISEN DRAMATICALLY.

"Coming up on Healthbeat: Find out about the relationship between salt and high blood pressure. That's next on Healthbeat!"

Across the country, gospel radio stations are carrying a new tune: They're telling listeners how to stay healthy and avoid cardiovascular diseases, including the number one health threat to African Americans—high blood pressure.

The messages are one part of a major new effort by the National Heart, Lung, and Blood Institute (NHLBI) to improve the health of African Americans, who suffer disproportionately from high blood pressure and stroke.

FACT: About a third of African Americans have hypertension, compared with a fifth of all Americans.

FACT: African Americans develop high blood pressure, or hypertension, at an earlier age than whites.

FACT: At every decade of life, African Americans suffer more *severe* high blood pressure than whites, and have higher rates of hypertension-related deaths.

FACT: By age 65, more than 70 percent of African Americans will have high blood pressure, compared with about 50 percent of whites.

Yet, as Dr. Patrice Desvigne-Nickens, an NHLBI scientist involved in the new effort, notes, "The reasons for African Americans' greater susceptibility to high blood pressure are multiple, complex, and little understood." Possible contributing factors include genetics, socioeconomic factors, and lifestyle.

Outreach Efforts Use Creative Approaches

One of the NHLBI's most innovative outreach efforts is its Healthbeat Radio Network, begun in 1993 and aimed at African Americans over age 25. Its 1 minute news and feature spots play on hundreds of gospel and news/talk radio stations across the United States.

For instance, one spot features Dr. Charles Curry of Howard University Hospital in Washington, D.C., telling listeners why salt can be dangerous. Then, retired teacher Marilyn Green offers tips on how she manages to keep her salt consumption within the recommended limit of no more than a teaspoon a day: "Basically I use saltless seasonings," she says, "like something from the parsley patch. Garlic and thyme, rosemary and paprika and pepper."

Other features emphasize the value of keeping a proper weight (about 20-30 percent of all hypertension in the United States is attributable to being overweight), of being physically active, and of not consuming too much alcohol (no more than two drinks daily is the recommended limit).

With Healthbeat's tips a big hit, the NHLBI has begun producing a new series of them.

Another innovative effort is the Stroke Belt Initiative, which brings crucial information on high blood pressure to the South, where 11 States have unusually high death rates from stroke—10 percent above the national average.

Uncontrolled hypertension is the major cause of stroke. Nationwide, African Americans have twice the death rate from stroke as whites. In the Stroke Belt, although African Americans and whites, men and women, have high death rates from stroke, the African American rate is highest—and higher than that of African Americans living elsewhere in the United States.

One of the most popular projects is "Strike Out Stroke," which has brought the hypertension message to baseball parks.

The Stroke Belt Initiative began in 1990, when the NHLBI funded 11 health departments in Stroke Belt States to start projects to help people lower their high blood pressure, reduce weight, and stop smoking—all key steps to prevent stroke. Projects involved churches and other community sites. State health departments trained volunteers, worked with the media, and developed easy-to-read health education materials.

STRIKE OUT
STROKE
STRIKE OUT
STROKE
STRIKE OUT
STROKE
Control Your
Blood Pressure and
STRIKE OUT
STROKE
A Cooperative Project
Of the University of Maryland Department of Family Medicine
Community Health Assessment and Monitoring Program CHAMP
Bon Secours Hospital and the
National Heart, Lung and Blood Institute
SCORECARD

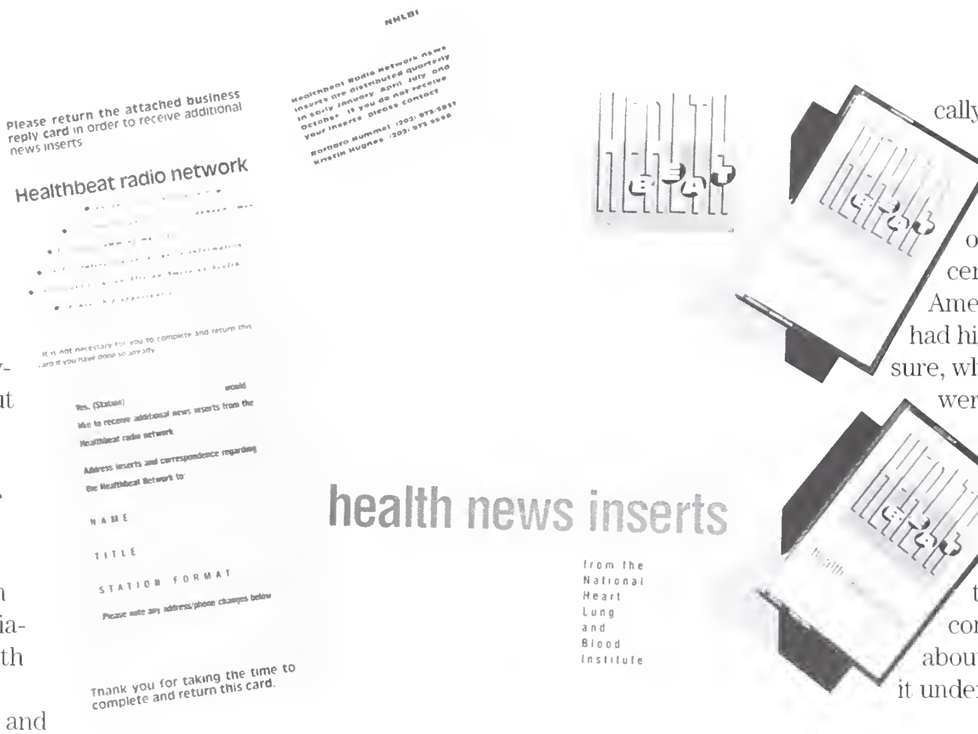
Those projects led to still others, one of the most popular being "Strike Out Stroke," which has brought the hypertension message to baseball parks. Messages appeared on scoreboards at half-time and booths offered free blood pressure tests and information. The campaign has scored big wins at games in Atlanta with the Braves and in Baltimore with the Orioles, as well as with minor-league teams in Mississippi and Arkansas.

In 1993, the NHBPEP launched a second phase of Stroke Belt projects. These provide opportunities to bring the message to still more people, as well as to evaluate new techniques to prevent stroke through improved high blood pressure detection and control.

Education Programs Aimed at Those Most at Risk

NHLBI also is trying to help those at risk now through a variety of educational outreach efforts. For example, in late 1993 the institute awarded five, 4-year grants under a new initiative called "Improving Hypertensive Care for Inner-City Minorities." The initiative seeks to develop and test strategies for encouraging people to be tested for and control their hypertension. Projects

HEALTHBEAT RADIO NETWORK PROVIDES NEWS AND FEATURES SPOTS AIMED AT AFRICAN AMERICANS OVER AGE 25.



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NHLBI

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Barbara Hummel (202) 973-5857
Kristin Hughes (202) 973-5858

will be conducted in various cities among African Americans, as well as other minority groups and low-income whites.

The NHLBI also disseminates life-saving information about high blood pressure through its National High Blood Pressure Education Program (NHBPEP). The NHBPEP works with major medical associations, voluntary health organizations, State health departments, and community groups to educate patients, health professionals, and the public about the prevention and treatment of high blood pressure.

In addition, several scientific initiatives are exploring the biological mechanisms underlying high blood pressure in African Americans, such as their greater sensitivity to salt. Other efforts are aimed at producing better ways of identifying those at risk for hypertension, so that early steps can be taken to prevent the disease or decrease its severity.

Recent data show that these and other outreach efforts are working. The percentage of African Americans who know they have high blood pressure (140/90 mm Hg or above) and are controlling their condition has risen dramatically in the past 15 years. A 1976-80 national survey found that only about 66 percent of African Americans knew they had high blood pressure, which means they were tested for it; less than 40 percent of hypertensive African Americans were treating their condition; and only about 13 percent had it under control.

A 1988-91 national survey shows the improvement:

- 73 percent of hypertensive African Americans are aware they have high blood pressure—the same as for the total U.S. population.
- 56 percent of hypertensive African Americans are having their high blood pressure treated—slightly better than the 55 percent for the total U.S. population.
- 28 percent of hypertensive African Americans have their condition under control—compared with 31 percent for all U.S. hypertensives.

Those data indicate that the messages are understood and hold the promise that strokes and other hypertension-related deaths among African Americans will drop.

Louise Williams, public affairs specialist, the National Heart, Lung, and Blood Institute.

Pima Indian children.

Minorities Benefit from Diabetes Research

Diabetes researchers have set out to learn why diabetes disproportionatley affects minorities, and to manage and prevent the disease.

In noninsulin-dependent diabetes mellitus (NIDDM), the pancreas produces insulin but for unexplained reasons the body cannot use the insulin effectively. The end result is the unhealthy build-up of glucose in blood and the body's inability to make efficient use of its main source of fuel. Since the end of World War II, the incidence of NIDDM in minorities has been rising at an alarming rate. The numbers speak for themselves:

- Native Americans have the highest rates of diabetes in the world: diabetes is seven times more common in Native Americans than Caucasians. In the Pima Indians, half of all adults have diabetes.
- African Americans comprise 12 percent of the U.S. population, yet they represent 20 percent of all diagnosed cases of diabetes. It is estimated that one in 10 African Americans will develop the disease.
- In Hispanics, nearly 10 percent of the adult population has diabetes. The number of Hispanics with diabetes is expected to increase because Hispanics are the fastest growing minority group in the U.S.

In light of these dramatic statistics, diabetes researchers supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) have set out to learn why diabetes disproportionately affects minorities, and to manage and prevent the disease. One thing is clear—those who are overweight are at high risk. Approximately 80 percent of people with NIDDM are overweight and obesity is a growing health problem in minorities. Other risk factors are genetic predisposition, advancing age, and poor socioeconomic status.

Studies have shown that Native Americans, Africans, and Hispanics living in their native homelands—where the traditional diet is low in fat—have very low rates of obesity and diabetes. When these minorities adopt a high fat diet and sedentary lifestyle, weight gain, and frequently diabetes and its complications, become significant health problems. For example, obesity and noninsulin-dependent diabetes mellitus did not appear at epidemic levels in the Pimas until after WWII, when the tribe integrated with Caucasians and started trading their handmade baskets for lard and flour. At the NIDDK Phoenix Epidemiology and Clinical Research Branch in Arizona, researchers have studied the Pimas since 1965 to learn more about the role of obesity in causing NIDDM and insulin resistance as a precursor to the disease.

Predicting Who Will Get NIDDM

Researchers know from longitudinal studies of the Pima Indians that insulin resistance runs in families. Research conducted last year on adults with high fasting insulin concentrations (hyperinsulinemia) showed that hyperinsulinemia in the presence of normal blood sugars indicates insulin resistance and predicts the development of NIDDM. Scientists wanted to know if children susceptible to NIDDM were hyperinsulinemic too, so they measured fasting insulin concentrations in non-diabetic Pima and Caucasian children. Their data showed that hyperinsulinemia appears in young children at risk for NIDDM as well. Research is now under way to determine if hyperinsulinemia plays a role in the development of microvascular disease, a long-term complication of diabetes.

In addition to showing that hyperinsulinemia predicts the development of NIDDM, scientists are gathering evidence to support their belief that genetic predisposition plays a role, and that environmental factors trigger the disease. Recently, genetic analyses of Pima siblings showed linkage between a position on chromosome 4q and a nearby gene believed to contribute to insulin action among them. The role of this gene appears to be distinct from genes or environmental factors that result in obesity, but further research is needed to learn more about its role in insulin action.

Diabetes Research and Training Centers Study Minority Health

Several of the Diabetes Research and Training Centers (DRTC) supported by NIDDK are focusing on minority health. The DRTCs train health care professionals and translate clinical research advances into improved care for people with diabetes.

The DRTC at Vanderbilt University in Nashville is investigating patterns of eating behavior in people with NIDDM. Researchers are evaluating dietary compliance in a group of obese African Americans who could improve their diabetes control by following a low calorie diet.

At the University of Chicago DRTC, a project originally developed to evaluate lifestyle modification for obese African American women with NIDDM has been applied to a Hispanic population. The project, called Pathways, assists inner city African Americans and Hispanic women in modifying their diets and adopting exercise programs for weight loss. Recently, one half of the group lost more than five pounds, a statistically significant achievement for a group that has difficulty losing weight.

NIDDK Launches Promising Research

Other promising research efforts at NIDDK are geared to preventing and managing diabetes in minority populations. In spring 1994, the institute funded grants for "Interventions in Diabetes Among Minority Populations," proposals solicited to reduce the public health burden of diabetes in African, Asian and Hispanic Americans, and Native Hawaiians and Pacific Islanders.

Later this year, NIDDK expects to recruit patients for a full-scale, randomized, multi-center clinical trial, "The NIDDM Primary Prevention Trial." The study will evaluate interventions designed to delay or prevent the onset of NIDDM in individuals at increased risk for developing the disease. Minorities will make up 50 percent of the study population. Minority women with a history of gestational diabetes and/or obesity will be an important component of this trial. NIDDK has concluded a pilot study in the Pima Indians to assess the effectiveness of exercise and diet in managing diabetes in this population. The diet/exercise intervention will be tested in a larger group of Pimas as part of the full-scale trial.

Lorraine Marchand, science writer/editor the National Institute of Diabetes and Digestive and Kidney Diseases.

Shortage of African American Oncologists Reflects Larger Problem

DR. OTIS BRAWLEY

> THE SHORTAGE IS DUE, AT LEAST IN PART, TO OBSTACLES THAT EXIST ALL ALONG THE WAY FOR MINORITEIS INTERESTED IN A CAREER IN SCIENCE OR MEDICINE.

There is a serious shortage of African American oncologists in this country. Of the more than 30 million African Americans in the U.S. today, fewer than 60 of them are board-certified oncologists.

"This situation reflects the larger problem of too few minorities in research and medical careers all across the board," explains Otis Brawley, M.D., a senior investigator at the National Cancer Institute and one of three African American physicians out of 104 graduates in the class of 1985 at the University of Chicago Medical School.

The shortage is due, at least in part, to obstacles that exist all along the way for minorities interested in a career in science or medicine—and many of them appear early.

According to some experts, the problem is largely one of education. Nelson Canton of the National Education Association in Washington, D.C. explains: About 40 percent of U.S. school children are minorities (50 percent in California). Unfortunately, about 30 percent of inner-city high schools with large minority enrollments have no physics classes and approximately 17 percent offer no courses in biology or chemistry, he said.

Educator Walter Sullivan, Ph.D., vice president for Health Promotion at Morehouse School of Medicine in Atlanta, Georgia, says, "There simply are not enough students being trained for careers in medicine and science. The problem has to be approached on different fronts. For a start, you have to expose children at a young age to science, provide them with the proper role models, and help them see what their possibilities are."

Even with training and encouragement many minority students are still not selecting research careers. "There is a tremendous disincentive for African Americans going into research— and it's primarily economic," explains Brawley. "When a typical student, African American or white, graduates from medical school, he or she often has a huge debt that must be paid back. The last thing minorities can afford to do is to invest in more training or take a job in a relatively low paying field, such as science. They may really want to do research, but they just can't afford it."

In 1993 legislation was passed that provides funds to pay off the educational loans of disadvantaged students, including minorities, interested in pursuing research careers. Specifically, the NIH has a program that will pay off the loans of qualified minority clinical researchers working at the NIH.

Brawley adds that African Americans remain outsiders in research careers not because they can't do the work, but because they don't have exposure to the environment or access to the connections needed to advance. He reminisces about his first experiences in a lab. "My dad worked in a hospital and from an early age took me to work with him so I could be around the people in the labs. I was sort of a 'forced volunteer' processing blood samples, but from this first exposure my interest in science grew."

For those not so fortunate to have early exposures to science, alliances between education and the scientific communities may provide the answer. Five years ago, the National Cancer Institute became one of the first of the NIH institutes to start an "Adopt-A-School Program." NCI adopted McKinley High School, an inner-city school in Washington, D.C. with a predominantly African American enrollment.

Students are selected by the school and attend monthly sessions where NCI scientists cover health and science topics for practical application as well as future career possibilities. Says Maxine Richardson, NCI's Equal Employment Opportunity program manager, "We're looking for students with potential, not necessarily those with the best grades. When they finish the program we want them to be inspired to do science."

Part of that inspiration occurs when students are brought to NCI to get a first hand look at modern biomedical research. For many this is the first time they are exposed to clinical research and molecular and cellular biology. At the end of the school year a small number of students are selected to participate in the summer program at NIH, where they work closely with NCI scientists, culminating in a poster session describing their work. Students are tracked to see if they select academic programs in science. The program may eventually serve as a model for other regions of the country.

Two years ago, NCI scientists under the direction of NCI Clinical Director Dr. Gregory Curt began an AIDS program, where minority students have an opportunity to learn about AIDS from NIH scientists and speak with AIDS patients at the NIH Clinical Center. "It puts a human face on this disease, so that students realize that AIDS patients are people like them," said Curt. AIDS awareness is a large component of the program, and to date, it appears to be increasing the students' understanding of the disease, he adds.

Programs such as these offer exposure to science and the skills to get started, yet, as Brawley states, "a glass ceiling still exists for minorities in science and medicine. Without the proper nurturing and guidance, it just doesn't happen for minorities. Unlike many minorities, I was fortunate enough to have several terrific mentors who encouraged me at various points throughout my career."

Reflecting on his specialty, Brawley adds, "Oncology, like many other areas in medicine, is a club. You have to know who can help you get in."

The rules of the club may be changing. In 1992, a little over one-fourth of the 16,000 students enrolled in U.S. medical schools were minorities, an increase over previous years. "This is certainly an encouraging trend, but we all need to do more," concludes Brawley. "If we don't find ways to help more minorities select and advance in research careers, we're shortchanging everyone."

Mary Sullivan, editor, ***NIH News & Features*** *magazine and Francis X. Mahaney, Jr., medical science writer, the National Cancer Institute.*

Centers Program Strengthens Research Capability of Minority Institutions

THE RCMI PROGRAM STRIVES TO ENHANCE AN INSTITUTION'S CAPACITY TO CONDUCT BIOMEDICAL AND BEHAVIORAL RESEARCH TO LESSEN THE DISPARITY IN HEALTH STATUS BETWEEN MINORITY AND WHITE AMERICANS.

Investigators at Drew University School of Medicine and Science in Los Angeles are working to improve a substance that helps premature infants suffering from respiratory distress syndrome (RDS) to breathe easier.

These infants have underdeveloped lungs that cannot produce lung surfactant, the substance that lines the inner walls of alveoli—tiny air sacs in the lungs—and prevents them from sticking together as they expand and contract with breathing. Lack of surfactant makes breathing a herculean, if not impossible, task.

The researchers recently found that surfactant protein B effectively holds in place surfactant lipids so that they form a thin film that does not dissipate under pressure similar to that encountered with breathing.

DR. ALAN WARING AND HIS ASSOCIATES AT DREW UNIVERSITY OF MEDICINE AND SCIENCE ARE WORKING TO SAVE THE LIVES OF THE 40,000 PREMATURE INFANTS BORN WITH RESPIRATORY DISTRESS SYNDROME (RDS) IN THIS COUNTRY EACH YEAR. BY DEVELOPING AN EFFECTIVE LUNG LUBRICANT THAT ALLOWS EASIER BREATHING, THE RESEARCHERS HOPE TO ALLEVIATE THE EFFECTS OF RDS, WHICH IS THE LEADING CAUSE OF DEATH FOR THESE BABIES.

This discovery could lead to a more effective surfactant substitute, which would translate to less suffering and lower mortality rates for these premature babies.

The researchers are participants in a National Center for Research Resources (NCRR) program begun in 1985. The Research Centers in Minority Institutions (RCMI) Program is geared to strengthen the research capability of predominantly minority educational institutions that offer doctorates in the health professions or health-related sciences. The RCMI Program strives to enhance an institution's capacity to conduct biomedical and behavioral research to lessen the disparity in health status between minority and white Americans.

"Historically, minority educational

institutions have trained many of the professionals who work to improve the health of minority communities. It only makes sense to strengthen these schools in order to continue that work," says Dr. Judith Vaitukaitis, NCRR director.

Obtaining research funding is a challenge for any biomedical investigator. For scientists at minority institutions, the difficulty is compounded by lack of adequate support for developing research infrastructures—the human, animal, technological, and other resources that underpin biomedical research.

RCMI helps fill this need. Program funds are used to renovate laboratories and animal facilities, develop multidisciplinary core research facilities, provide support for faculty development and expansion, and state of the art equipment, and enhance collaboration among researchers.

The program has so far supported 19 grantees at seven medical schools, three colleges of pharmacy, eight graduate schools, and one school of veterinary medicine. Initial funding for the program was $43.9 million which grew to $119.4 in 1992, a 172 percent increase.

A measure of the program's success is seen in the area of AIDS and AIDS-related research. In 1988, RCMI grantees received about $618,000 for AIDS research. By 1992, that amount had increased to $14 million, a 2000 percent rise. This advance is attributed to the improved research infrastructure through RCMI support, and to collaboration with the National Institute of Allergy and Infectious Diseases.

With RCMI support, Dr. Georgia Dunston established an immunogenetics laboratory at Howard University. She is currently expanding the laboratory to create a genetic database of African-American pedigrees, which will provide valuable information to researchers mapping the entire human genome. (Photo by Jefferey John Fearing, Howard University College of Medicine).

The Ponce School of Medicine in Puerto Rico had little in the way of research resources—let alone facilities to support quality AIDS research—before obtaining an RCMI grant in 1985. Ponce was able to recruit immunologist **Dr. Yasuhiro Yamamura**, who is conducting a study of HIV transmission from pregnant Puerto Rican women to their fetuses.

Approximately 30 to 35 percent of infants born to HIV-positive mothers are infected themselves. AIDS development in the newborns is rapid; disease and death follow quickly making early and accurate diagnosis imperative.

Dr. Yamamura and his colleagues are evaluating the time sequence associated with HIV transmission from mother to child. By measuring levels of maternal HIV antibodies in the mother's blood and the umbilical cord at childbirth, they have discovered that not all maternal antibodies pass through the placenta equally well, and that transport of HIV antibodies varies from patient to patient.

Dr. Clivel Charlton and his team at Meharry Medical College have developed a new animal model based on normal human physiology to study Parkinson's disease (PD). Charlton says this model involves compounds produced in humans—unlike most models—and can explain the total biochemistry of PD. (Photo by Karen Moore Fears, Meharry Medical College)

Dr. Yamamura is working to identify the protective elements of maternal antibodies, and then determine the immunologic factors that prevent or permit HIV infection of the fetus.

Enabling this type of collaboration is a major goal of the RCMI program. Some of the new partnerships are expanding important areas of research.

In partnership with the National Center for Human Genome Research, **Dr. Georgia Dunston** is expanding the RCMI-supported **Human Leukocyte Antigens (HLA) typing laboratory at Howard University in Washington, D.C.**

Dr. Dunston hopes to establish an organized collection of African American family histories and corresponding DNA samples. This genetic data will allow scientists to identify gene-based differences already known to exist among population subgroups. Some of these differences are sensitivity to drugs, tissue rejection in organ transplants, and environmental influences on health and susceptibility to disease.

Dr. Clivel Charlton, who was recruited via RCMI support to **Meharry Medical College in Nashville, TN,** has developed a new animal model for studying Parkinson's disease (PD). Dr. Charlton's work is supported by the National Institute of Neurological Disorders and Stroke, and the National Science Foundation. His team has produced Parkinson-like symptoms in rats by injecting them with S-adenosyl-L-methionine (SAM)—an overproduction of which is a suspected cause of PD.

L-dopa frequently is used to treat PD, but loses its efficacy over time. The Meharry researchers found that continued administration of L-dopa increased SAM production in the rats, renewing the PD-like symptoms. Dr. Charlton's results suggest that SAM-induced hypokinesia—loss of motor coordination—may actually be involved in the etiology of Parkinson's disease.

Putting the program into perspective, Dr. Sidney A. McNairy, Jr., RCMI director, says that "when the goals and objectives of the program are realized, we will have established centers of excellence for biomedical research that *happen* to be at minority institutions." "When that day comes," he adds, "we will be close to eliminating the disparity in the health status of our minority and white populations. I believe that the RCMI grantee institutions are being positioned to become key players in our nation's health agenda as we move closer to the year 2000."

Kathleen Canavan, public affairs specialist, formerly with the National Center for Research Resources.

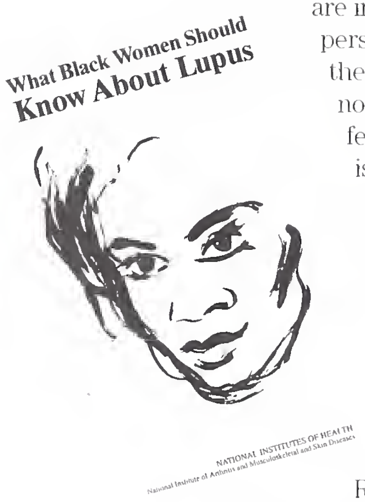
Research Provides Benefits to Minorities with Lupus

LUPUS IS THREE TIMES MORE COMMON IN AFRICAN AMERICAN WOMEN THAN WHITE WOMEN, AND THE MORTALITY RATE IS MUCH HIGHER.

Why is systemic lupus erythematosus (SLE) more common in African American women than in white women in the United States? Why does lupus strike women more often than men? What causes this disease? How can we improve its diagnosis and treatment? These are some of the questions that the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) is addressing in stepped-up efforts to conquer this complex disease.

Lupus primarily affects women of childbearing age, at a ratio of nine women to each man. The disease is three times more common in African American women than white women, and the mortality rate for African American women is much higher. Lupus occurs in as many as 1 in 250 African American women.

In lupus, regulation of the immune system goes awry, and the body produces autoantibodies—antibodies that attack the patient's own tissues. This autoimmune reaction, as it is called, results in inflammation that causes redness, pain, and swelling in affected parts of the body. Most often the joints, skin, kidneys, lungs, heart, nervous system, and blood vessels are involved. The signs and symptoms of lupus differ from one person to another, but can include a red rash or color change on the face, often in the shape of a butterfly across the bridge of the nose and cheeks. Other signs are painful joints and unexplained fever. The disease can range from mild to life-threatening, and is characterized by periods of flare-up and remission.



What Black Women Should Know About Lupus

NATIONAL INSTITUTES OF HEALTH
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Causes: New Clues

Although the causes of lupus are not completely understood, the disease is believed to result from an interplay of genetic, environmental, and hormonal factors. Studies aimed at understanding why lupus is more common in certain ethnic groups, as well as in women, should enhance understanding of the disease in general, and may yield clues on how to treat it in different populations.

Research has provided a much clearer understanding of the genetic basis of lupus. Scientists have identified specific immune system genes that are associated with susceptibility to the disease, and identifying individuals who carry these genes may enable successful preventive measures to be developed. In addition, better understanding of how certain genes predispose an individual to lupus may lead to new treatments.

An exciting area of research indicates that lupus may involve defects in a process by which the body eliminates unnecessary, damaged, or potentially harmful cells. This process is known as programmed cell death or apoptosis. In the immune system, apoptosis is responsible for eliminating white blood cells with the potential to react against the body's own tissues. Normally, the immune system detects these "self-reactive" cells, and they are destroyed by apoptosis before they can do any harm. If the process of apoptosis is defective, self-reactive cells will survive and may cause autoimmune diseases such as lupus.

Recent NIAMS-supported studies show that, in a mutant mouse strain that develops a lupus-like illness, one of the genes that controls programmed cell death is defective. When this defective gene, called *fas,* is replaced with a normal *fas* gene, the mice no longer develop signs of disease. Preliminary research suggests that defects in apoptosis may also occur in people with lupus. Better understanding of the role of apoptosis in lupus may lead to new, targeted treatments for this disease, perhaps even through gene therapy.

For many years, doctors have observed that people with lupus are excessively sensitive to sunlight; even a short time spent in the sun without protection from harmful ultraviolet (UV) rays can cause the disease to worsen or flare suddenly in some people. Researchers investigating the mechanisms by which lupus is exacerbated by UV light found that skin cells from people with SLE are more sensitive to UVB rays than skin cells from other people. Exposure to UVB light causes certain proteins normally found in the cell's nucleus to accumulate in abnormally large amounts on the cell surface. These proteins react with autoantibodies commonly found in people with SLE. A better understanding of the mechanisms of sun sensitivity in lupus may enable development of ways to prevent the harmful effects of the sun in lupus patients.

Pregnancy: No Longer Contraindicated

Twenty years ago, medical textbooks said that women with lupus should not get pregnant, because of potential health risks to both the mother and unborn child. For reasons not entirely understood, women with lupus often have miscarriages or give birth very prematurely. Today, although lupus pregnancies are still considered high risk, with proper medical care most patients can have safe pregnancies and carry their babies to term.

Research has led to increased understanding of the factors associated with lupus-related miscarriages, such as two closely related autoantibodies known as antiphospholipid antibody and lupus anticoagulant. About one-third of lupus patients have these antibodies, which can be detected by simple blood tests. Detection of these antibodies can alert physicians to take measures to try to prevent miscarriage in these patients.

In related work, researchers have identified a new type of lupus—neonatal (newborn) lupus—that can be associated with complete heart block in some affected babies. Babies born with this serious defect in heart function often die; others suffer permanent injury of heart tissues, often requiring lifelong use of a pacemaker. Women who are at risk for giving birth to children with neonatal lupus can now be identified by detecting the presence of specific lupus autoantibodies known as anti-Ro or anti-SSA in their blood, enabling steps to be taken to treat heart block if it occurs in their babies.

Doctors also are able to much more clearly define the various stages of lupus and to identify different disease syndromes within the larger category of lupus. The understanding that this is not a single disease, combined with refinements in the way lupus in its various forms is treated, enables doctors to devise treatments that are more tailored to the individual.

Treatment: Novel Approaches

Because the signs of lupus vary from one person to another, treatment must be individualized to the patient. Drug treatments may include aspirin or nonsteroidal anti-inflammatory drugs to control fever and pain and swelling in the joints. Cortisone-like drugs also may be given. In severe cases, more powerful agents that suppress immune system activity may be used.

Recent NIAMS-sponsored studies in mice that develop a lupus-like autoimmune illness indicate that nitric oxide, a natural substance known to promote inflammation, plays a role in causing disease symptoms. These mice, which have inflammation of the joints and kidneys, were found to produce abnormally high levels of nitric oxide in their tissues. When the mice were treated orally with a drug that blocks nitric oxide formation, development of kidney disease was prevented and joint inflammation was reduced. Additional studies are needed to determine whether nitric oxide plays a role in inflammatory disease in humans, and whether drugs that block the formation or action of nitric oxide will be valuable in treating patients with lupus.

Research conducted and supported by the NIAMS has led to important advances in the treatment of people suffering from lupus, resulting in significant improvements in the quality of life for these patients. For example, a drug regimen developed at the NIH can delay or prevent the development of kidney failure in patients with lupus nephritis (inflammation of the kidney), one of the most serious complications of lupus. An analysis done by the NIAMS shows that in one year, this treatment regimen saves the entire cost of its development (about $9.5 million) by preventing or delaying cases of kidney failure.

Much research remains to be done before the disease can be successfully treated or prevented. NIAMS has awarded several new grants for studies on the causes and mechanisms of tissue injury in lupus and on why the disease strikes women and certain minority populations more frequently. In addition, the institute has just established the first two Specialized Centers of Research (SCORs) ever devoted to lupus. These centers, at the Hospital for Special Surgery at Cornell University in New York City, and the University of North Carolina at Chapel Hill, will enable collaborative research on lupus between basic scientists and clinicians.

Elia Ben-Ari, science writer, the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Increase in Minority Organ Donors Goal of New Education Program

The need for donated organs and tissues among minorities is critical. Minority individuals represent 42 percent of the nation's 32,000 patients on transplant waiting lists, but only 22 percent of organ donors are minorities. Increased rates of insulin-dependent diabetes, hypertension, chronic renal failure, and lupus erythematosus contribute to the need for kidney and heart donors in particular.

Since organs and tissues are more likely suited for transplantation when donors and recipients are of the same ethnic background, the scarcity of minority organ donors has serious consequences for the health and quality of life of these individuals.

"It has become apparent that society as a whole, and minorities in particular, need to be better educated about the importance of organ donation," says Dr. John Ruffin, ORMH director. "The Minority Organ Tissue and Transplant Education Program (MOTTEP) provides focused information to the minority community—information that we expect will lead to an increase in the number of minority donors."

First year funding of $400,000 by the Office of Research on Minority Health established 3 regional sites for community-based organ/tissue donor education programs. During the program's second year, an additional $800,000 will allow for new sites in Atlanta, GA; Chicago, IL; Honolulu, HI; Houston, TX; Nashville, TN; Brooklyn, NY; Salt River Pima Reservation, AZ; and Washington, D.C., and maintain existing sites in Birmingham, AL; Cleveland, OH; and Los Angeles, CA.

DR. CLIVE CALLENDER

MOTTEP is an outgrowth of the pioneering efforts begun in 1982 by the D.C. Organ Donor Program, sponsored by the National Kidney Foundation of the National Capital Area and Howard University Hospital, and the "Take Initiative" Program of the Dow Chemical Company.

"The intent of the MOTTEP program is to employ as coordinators persons of African American, Hispanic, Native American, or Asian descent who will organize their communities and educate them to increase organ donation rates in their areas," says Dr. Clive Callender, principal investigator and director of Howard University's transplant center since 1973. The coordinators, who themselves may be transplant recipients and individuals on waiting lists, will assess the specific educational needs of each group, and prepare information not only related to transplantation but a variety of health care issues.

Several factors contribute to the lack of participation of minorities in transplant programs. Says Joel Newman of the United Network for Organ Sharing (UNOS), "Many minorities feel they have less access to health care in general, and are not likely to get an organ if they need one. 'So why donate an organ to someone else?'," they ask. Many have cultural or religious concerns about donating, and some also fear that if they sign donor cards and subsequently are involved in a life-threatening emergency, hospital personnel will not work to save their lives, he says.

"Speculation continues that transplantation as a treatment option is not offered as often to non-white patients,"

> MOST PEOPLE ARE AWARE OF THE SUCCESSES OF ORGAN TRANSPLANTATION, BUT MOST REMAIN UNAWARE OF THE NEED THAT EXISTS FOR MINORITY ORGAN AND TISSUE DONORS.

says Karen Smith of the Division of Organ Transplantation in the DHHS Health Resources and Services Administration. "Also, family members often worry that they will not receive the same quality of care as whites, and there is a known disparity between the length of time African Americans and whites wait for their first kidney transplant, with African Americans waiting almost twice as long."

Everyone has to become educated, says Smith. The nation is experiencing such rapid growth in minority populations that "cultural awareness and sensitivity, especially related to minority communities, must be taken into account when dealing with health issues, particularly organ and tissue donation. There are a lot of differing perceptions of these issues out there that must be considered," she says.

Both Smith and Newman support MOTTEP. They agree that although most people are aware of the successes of organ transplantation, most remain unaware of the need that exists for minority organ and tissue donors.

For example, a disproportionate number of African Americans suffer from end stage renal disease (ESRD), and data from the NIH-supported U.S. Renal Data System shows that, in 1988, the incidence of ESRD was 3.7 times higher among African Americans than whites. While African Americans represent about 12 percent of the U.S. population, 26 percent of new kidney registrants on the transplant waiting list in 1991 were African American, while 22 percent of kidney recipients were African American.* As of October 1993, 33 percent of all patients awaiting kidneys were African American.

What are the overall benefits which Dr. Callender, Dr. Ruffin, and others are looking for from MOTTEP? Says Dr. Callender, "We want to increase the percentage of organ/tissue donations in minority communities by developing effective education strategies that reach every major minority group. We want to create strong volunteer community programs which empower minorities to be part of an overall improved health care system. And we want to help save the millions of dollars spent each year in health care costs due to the lack of minority donors."

Dr. Callender is encouraged by the interest and support MOTTEP has received thus far. Working together with the American Society of Minority Health and Transplant Professionals (ASMHTP), he says, "the program provides a unique opportunity for transplant and health care professionals to interact directly with communities to improve the health and quality of life for all Americans, especially minority Americans."

** 1993 Annual Report, U.S. Scientific Registry of Transplant Recipients and the Organ Procurement and Transplantation Network, UNOS*

Bernardine A. Moore, supervisory public affairs specialist, and Chief, NIH Public Information Branch.

Illustration by Elizabeth Wolf

Research Seeks to Understand Multicultural Speech and Language Development

Cultural diversity is a heritage that Americans share. At the heart of diversity is difference in language. Language enables individuals of a culture to interact and belong, and while language bonds individuals to their culture, it also separates them from others.

The majority of Americans speak Standard American English (English). The 1990 U.S. Census, however, identified approximately 32 million people ages five years and older who speak a non-English language in their home. They comprise almost 14 percent of the population. Many live and work in ethnic communities where English is the "minority language." Many others, however, decide to live or seek employment outside their ethnic community.

While it is important to maintain America's heritage of cultural diversity, and therefore preserve language differences, it is also important for most individuals to successfully learn and speak Standard American English, the majority language. The National Institute on Deafness and Other Communication Disorders (NIDCD) supports research investigating how speech and language are acquired and developed, which includes the ability of children and adults to learn a second language.

At the core of the ability to speak a second language is the ability to detect the fine differences between the speech sounds, or phonemes, of that language. For example, the words "pen" and "pin" differ by only one vowel. While native speakers of English have no difficulty detecting or pronouncing the difference between these similar yet distinct words, nonnatives may be unable to detect or produce the fine phonetic difference. They may confuse the two words and may also have difficulty pronouncing them.

Language Recognition Occurs Early in Life

At what age do individuals learn to hear the differences between the speech sounds of their language? NIDCD-supported scientists from the University of Washington in

Seattle examined the ability of infants to detect variations of similar yet distinct vowels from two different languages. These scientists discovered that babies as young as six months of age listen uniquely to sounds of their native language. The babies in this study recognized variations of a vowel sound in their native language, but were unable to detect similar variations of a foreign vowel sound. This suggests that the ability of six-month-old babies to perceive speech sounds has been altered as a result of the speech to which they have been exposed.

AT THE CORE OF THE ABILITY TO SPEAK A SECOND LANGUAGE IS THE ABILITY TO DETECT THE FINE DIFFERENCES BETWEEN THE SPEECH SOUNDS, OR PHONEMES, OF THAT LANGUAGE.

The scientists further suggest that as individuals continue to mature, speech perception becomes narrowly focused to the native language. It is this narrow focus that makes it difficult for adults to detect differences between the speech sounds of a foreign language and therefore speak that language without an accent. This may explain, for example, why many adult Japanese speakers learning English have difficulty discriminating the difference between "l" and "r."

It is possible, however, to learn to distinguish the fine differences between similar speech sounds of a foreign language. For example, NIDCD-supported scientists at the Indiana University in Bloomington investigated a new training procedure they developed to teach native Japanese speakers to detect the differences between similar words containing "l" and "r." In this study, native Japanese speakers had to discriminate between more than 200 very similar word pairs, such as "lead-read," that differed only by substitution of "l" for "r" or "r" for "l". The large number and variety of word pairs used in this highly structured training procedure along with immediate indication of a correct or incorrect response helped the Japanese speakers learn to detect the differences between the "l" and "r" words in the pairs.

Scientists Study Children Who Learn a Second Language

The question often asked is, "When is the best time to learn a second language?" Many experts suggest that the best time is during early childhood when the ability to learn a language comes naturally. Others argue that exposing a young child to more than one language will sacrifice proficiency in either language. They say it is better to learn one language well before attempting to learn another.

Scientists at the University of Miami are exploring the language performance of children who speak more than one language. The scientists recently examined the vocabulary skills of Spanish and English-speaking first grade students. Those bilingual children who spoke only Spanish in the home as well as those who spoke both Spanish and English performed equally well on Spanish vocabulary recognition tests. In addition, the children who spoke English and Spanish in the home scored higher on the English vocabulary recognition test than bilingual children who spoke only Spanish in the home. This finding suggests that learning two languages at once does not harm the ability of children to understand language and that it may actually help children learn the second language. It is important to note, however, that the English vocabulary of the children who spoke English and Spanish in the home was in the low-average range, while their Spanish vocabulary was comparable to those children who spoke Spanish only. This suggests that bilingual children may not have equal proficiency in both languages. It is important, therefore, that language tests for bilingual children include an evaluation of both their languages.

Unfortunately, there is a lack of standardized multicultural language tests in the United States. Because of this, many bilingual children are falsely identified as language impaired when actually their language is inadequately evaluated. Appropriate testing of language and proper academic placement are critical if multicultural children are to reach their full academic potential.

Awareness of the problem has prompted the NIDCD to issue a program announcement to stimulate research for the "Identification and Treatment of Childhood Language Impairment in Multicultural Populations." Program announcements alert scientists to an area of needed research even though funds have not been set aside for that research. Studies are needed to define and characterize impaired language in specific cultures at varying ages. New research is required to develop tests that will differentiate between language differences and language disorders across cultural groups, and to improve language treatment for language-impaired children from multicultural homes.

NIDCD conducts and supports a program of research and research training in speech and language, hearing, balance, smell, taste, and voice. NIDCD's goal is to make important contributions to the body of knowledge needed to help those who experience communication disorders and to advance research in all aspects of human communication. This goal includes encouragement and support for research involving multicultural communication.

Jo Bagley, technical writer/editor, the National Institute on Deafness and Other Communication Disorders.

New Program Helps Minority Students by Supporting Academic Collaboration

An innovative NIH program that supports academic collaboration is assisting minority students in crossing academic "bridges" critical to their future careers in biomedical research. Producing a new cadre of scientists is seen as an important step to promoting further interest in minority health, and ultimately closing the gap that currently exists between the health of minorities and the rest of the population.

"Bridges to the Future" began in 1992 after an NIH fact-finding team revealed that minority students often have difficulty with two key transition points in their education: the transition from the associate degree to the baccalaureate degree and from the masters to the doctorate degree.

"We know that many bright minority students attend two-year colleges, mainly because of financial reasons," says Dr. John Ruffin, director of NIH's Office of Research on Minority Health. "We wanted to provide a mechanism that enables students to continue their education and receive the support and training they need to further their research careers."

Minority students are underrepresented in biomedical research and at every level of science education. For example, although African Americans make up 12 percent of the population, they comprise fewer than 3 percent of the nation's doctors and less than 1 percent of its biomedical researchers. Hispanic Americans, one of the fastest growing ethnic groups in this country, comprise only 5 percent of the nation's doctors and 2 percent of scientists.

The bridges program works by supporting collaboration between minority and majority academic institutions. Specifically, the program encourages partnerships between institutions with significant minority enrollment that offer only an associate degree and colleges and universities that award the baccalaureate degree—the 2-year to 4-year bridge. The M.S.-Ph.D. bridge involves minority institutions that offer the master's degree as their highest degree and institutions that grant doctoral degrees.

"The idea behind the bridges program is to design a partnership or enhance an existing one, and to assist the institution that grants the lesser degree the opportunity to increase its academic competitiveness," says Dr. Americo Rivera, NIGMS program administrator for "Bridges to the Future." The program is funded by the Office of Research on Minority Health and administered by the National Institute of General Medical Sciences (NIGMS).

In addition to providing financial assistance to minority students, the program may take a variety of directions including providing practical laboratory experience at the baccalaureate institution, establishing mentoring programs with faculty at the 4-year institution, supporting research collaborations and joint seminars between institutions, sponsoring visiting lectureships, and providing academic counseling.

To date, a total of 54 grants have been awarded, totaling almost $20 million, with three-fourths supporting the 2-year to 4-year bridge. Each grant is designed differently, depending on the school's resources, problems, and needs.

At Howard University in Washington, D.C., students participate in a 6-week program in math and science that prepares them for entrance into a baccalaureate science degree program. "We try to catch them early before they've made up their minds about a career," explains Dr. Winston Anderson, professor of biology and director of the bridges program at Howard. "Most students who are exposed to science at this time (after their second year in college) usually decide to continue on. It's very encouraging." In addition to including neighboring Maryland community colleges in Prince George's and Montgomery Counties, the bridges program at Howard has recently been expanded to include community colleges in Dade County, Florida in an effort to increase the presence of Latino students on the Howard (a predominantly African American) campus.

Building trust and credibility with the local Native American students who attend one of the six area community colleges means the difference between success or failure for the bridges program at New Mexico State University. Says Dr. Glenn Kuehn, professor of biochemistry, "Native Americans are very family-oriented. Many are reluctant to travel far from their reservation. In addition to providing the academic environment they need, we try to extend ourselves as individuals to them so they feel comfortable approaching us for help when they need it."

A broad-based research experience is the goal at San Francisco State University, where the school is one of the few that participates in both bridges. Master's students from Bay area colleges and universities can fill in the gaps in their research training and make up deficiencies that would otherwise prevent them from continuing in their research careers. "This is one of those rare programs that offers support for master's level students, allowing them to focus on their studies and eventually go on for their doctorate (at the University of California, Davis)," explains Dr. Frank Bayliss, professor of biology at San Francisco State. "Ultimately some of these students will be groomed for faculty positions."

IN ADDITION TO PROVIDING FINANCIAL ASSISTANCE TO MINORITY STUDENTS, THE BRIDGES PROGRAM MAY TAKE A VARIETY OF DIRECTIONS INCLUDING PROVIDING LABORATORY EXPERIENCE, ESTABLISHING MENTORING PROGRAMS, SUPPORTING RESEARCH COLLABORATIONS, AND PROVIDING ACADEMIC COUNSELING.

Perhaps one of the greatest benefits to be derived from the bridges program is the opportunity to expose minority students, many for the first time, to the range of career options available to them. "A large number of minority students think that law or medicine are the only professions they can enter in order to be considered a success," explains Dr. Bayliss. "We're trying to broaden their perspective to include a career in scientific research. Only about a third of the freshman and sophomore students demonstrate an interest in a basic science career. We're hoping that programs like 'Bridges to the Future' will change this."

Mary Sullivan, editor, ***NIH News & Features*** *magazine.*

Researchers Write Primer on Challenges of Minority Recruitment

MINORITIES ARE DISPROPORTIONATELY REPRESENTED AMONG THOSE WITH AIDS. YET THE NUMBER OF MINORITY PATIENTS IN CLINICAL TRIALS FOR HIV INFECTION HAS REMAINED DISPROPORTIONATELY LOW.

One of the greatest challenges facing AIDS researchers today—besides trying to find viable treatments and a cure for the disease—is the recruitment and retention of minority patients for clinical trials.

With the epidemic moving swiftly, inclusion of these patients in clinical trials is particularly urgent.

Two investigators supported by the National Institute of Allergy and Infectious Diseases (NIAID), Wafaa El-Sadr, M.D., M.P.H., and Linnea Capps, M.D., M.P.H., both of Harlem Hospital and Columbia University College of Physicians and Surgeons, have published a primer on "The Challenge of Minority Recruitment in Clinical Trials for AIDS" in the *Journal of the American Medical Association* (Vol. 267, No. 7, 1992).

The article focuses on the socio-economic factors responsible for the difficulty in getting African Americans who are poor and live in urban areas to participate in clinical trials for HIV infection. The authors acknowledge that some of these factors may apply to other racial groups as well.

A researcher's goal is to achieve minority representation in clinical trials that mirrors their representation in the community, explains George W. Counts, M.D., of the NIAID Office of Research on Minority and Women's Health. Data from all ethnic groups are essential to answer questions, about possible differences in clinical results based on race, he adds.

"This new model," says El-Sadr, "must reflect the special needs of these communities and should recognize and meet head-on the historical distrust of clinical trials—particularly among African Americans—and the need for extensive educational and social support services."

Minorities are disproportionately represented among those with AIDS. While African Americans comprise 12 percent of the U.S. population, they are 32 percent of all adult AIDS cases. In addition, Hispanics comprise 9 percent of the U.S. population and 17 percent of all adult AIDS cases. Together these two groups constitute 50 percent of the 401,749 reported cases of AIDS.

Yet the number of minority patients in clinical trials for HIV infection has remained disproportionately small. This underrepresentation is apparent in the literature reporting landmark studies on treatments against AIDS and its complications. Also, some studies show no racial breakdown of participants.

El-Sadr and Dr. Capps say successful recruitment requires an extensive educational effort. The authors emphasize that an explanation of basic research terminology is essential. A prospective participant must understand the meaning of a trial, random sampling, the nature of blinding, the concept of a placebo and a description of the responsibilities of the patient and the provider.

Only after a patient has a full understanding of these issues should the specific protocol be discussed. The researchers believe that many of the widely available educational materials lack cultural sensitivity and consideration of socioeconomic factors.

Researchers must accept that successful recruitment is more than supplying the study drug, they explain. It may mean providing a hot meal or meal vouchers, meeting transportation needs, providing social support and information on housing and substance abuse programs, or providing child care.

“This is a time-consuming process for researchers and staff,” they caution. “It requires educational skills, patience, and the building of trust.”

For example, at Harlem AIDS Treatment Group—one of NIAID’s Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA) centers—innovative services complement research protocols. A videotape and pamphlets address the concerns of the African American patient about clinical trials. Peer groups for clinical trial participants encourage patients to follow the research protocol and provide personal testimonies for others who may be interested in joining the trial. The services of a social worker and outreach worker are available. A van provides transportation to the clinic.

Research participants are incorporated into a system that attempts to meet multiple personal needs. Failure to fulfill these needs, warn El-Sadr and Capps, will doom well-meaning attempts to recruit and retain minorities in clinical trials.

“The compelling scientific, ethical, and social reasons for inclusion of minorities in clinical trials justify the necessary efforts to accomplish this important goal,” the authors conclude.

James Hadley, public affairs specialist, the National Institute of Allergy and Infectious Diseases.

AIDS Centers Use Recruitment Techniques to Increase Minority Enrollment

Many of the recruitment techniques outlined by El-Sadr and Capps are employed already by the 16 CPCRA or Community Programs for Clinical Research on AIDS sites.

“Each site usually provides a recruitment and retention plan as a part of their application,” Lawrence R. Deyton, M.S.P.H., M.D., chief of the HIV Research Branch of NIAID’s Division of AIDS, explains. “However, NIAID does not require, nor dictate how recruitment is to be accomplished. What works at one site may not work at another. Principal investigators and their respective personnel are better suited to make these decisions.”

“CPCRA sites are bringing the opportunity to participate in clinical trials to many people with HIV,” says Dr. Deyton. “They have shown a steady increase in minority enrollment since 1989,” he adds.

Data from CPCRA studies since 1990 reveal that nearly 37 percent of participants are African Americans and about 14 percent are Hispanics.

Another AIDS research network, the AIDS Clinical Trials Group (ACTG) has a more difficult time attracting minorities into clinical trials. Some academic and hospital settings, such as those used in the ACTG studies, may not be accessible to many patients, according to El-Sadr and Capps. The traditional research setting takes people out of their neighborhoods, they said.

In Fiscal Year 1990, 16 of the ACTG sites received supplemental funding from NIAID to recruit more minorities. Of those 16 sites, 11 received additional funding from NIAID and the National Institute on Drug Abuse to recruit injection drug users (IDUs).

Starting in Fiscal Year 1992, the ACTGs were required to have a viable plan to add a representative portion of minorities, women, and IDUs.

“We expect continued improvement in minority recruitment at the ACTG sites,” says Dr. Counts. Since 1987, the percentage of ACTG participants who are African Americans has risen from 6.5 percent to 26 percent, and Hispanics from 10.6 percent to 16 percent.

Researchers Recruit African Americans for New Study of Menopause

Purnell Cofield, one of the first African Americans to join a study of menopause at the National Institute on Aging (NIA), had a very definite reason for signing up: "I used to hear horror stories about menopause," says Cofield, "how women became so moody and cranky. But whenever I asked if it happened to all women, or what does actually happen, nobody had any answers. It's a subject I have a great interest in—being a woman and around that age—and I'd like to get some answers."

Cofield's personal reasons for enrolling in this study are strikingly similar to the scientific rationale supporting it: Very little is known about menopause. Medically, menopause has been defined as the point at which a woman has been without a period for one year. But what actually happens physiologically in the time leading up to that point—a span of years known as the perimenopause—is understood only in broad outline.

The study that Cofield has joined, known as the Perimenopausal Initiative, will fill in many of the details by following 100 African American and 100 white women as they pass through this midlife transition. One of the study's major goals is to chart the differences and similarities in the perimenopause among African Americans and whites.

"We know that there are changes in hormone levels well before menopause," says Jordan Tobin, M.D., who heads the study at the NIA's Gerontology Research Center (GRC) in Baltimore, MD. "But we want to find out precise details and rates of change—what happens, to which hormones, and when. We also need to relate these changes to body composition and bone density."

Body composition, the proportion of fat to lean on a person's body, tends to shift toward more fat with age. For women, the change can be rapid around the time of menopause. One of the many questions to be explored in this study is exactly how body composition interacts with hormone levels in African Americans and whites.

RITA PROCTOR, A PARTICIPANT IN THE BALTIMORE LONGITUDINAL STUDY OF AGING, HAS HER BONE DENSITY MEASURED. THE BLSA'S PERIMENOPAUSAL INITIATIVE WILL HELP EXPLAIN WHY AFRICAN AMERICANS HAVE A LOWER RISK OF OSTEOPOROSIS THAN WHITES.

According to co-investigator Michele Bellantoni, M.D., the study will be looking at several hormones. "We know that estrogen and body composition are related—women with more fat tend to have higher levels of one kind of estrogen—but we think that other hormones may be important as well. We're especially interested in the interaction of growth hormone and the reproductive hormones and how that interaction relates to body composition."

Bone density is another factor that intrigues Tobin and Bellantoni. Menopause brings a faster rate of bone loss in women, increasing their risk of developing osteoporosis. Common among older women, especially whites, osteoporosis is a condition in which

> One of the many questions to be explored in this study is exactly how body compostion interacts with hormone levels in African Americans and whites.

bones become fragile and break easily.

The study will measure bone loss in several different parts of the body, trying to find out when the rate of loss speeds up and how this change ties in with changes in hormone levels, muscle strength, physical activity, and other factors. The investigators hope the data will also throw light on why the rate of bone loss quickens around menopause but then slows down again a few years later.

Numerous other questions surround bone density and menopause. Why do African American women, for example, have a lower risk of osteoporosis than white women? "On the average, African American women start out with higher bone densities," says Bellantoni, "which may be one reason. But it could be that African Americans don't lose bone as quickly as whites because of other factors. We don't know all the reasons yet."

Recruitment Strategies

To recruit African American women, researchers are pursuing two broad strategies. In one approach they are focusing on African American organizations and community groups in the Baltimore area. Churches, historically Black colleges and universities, and newspapers with primarily African American audiences are key recruitment channels, according to the NIA's Barbara Hiscock.

The other major strategy—a simple but important one—is word of mouth. The Perimenopausal Initiative is part of a much larger study, the Baltimore Longitudinal Study of Aging (BLSA), which has used this strategy successfully to increase minority enrollment for both men and women of all ages.

"Currently about 12 percent of the active women participants in the BLSA are African American, up from just three percent 2 years ago," said Hiscock, who is senior operations manager for the larger study. "Most of this increase is through personal referrals. Our current participants often leave here with a handful of brochures to give to their friends, or they give us leads to people we can contact."

Recruitment for the Perimenopausal Initiative is a particular challenge, though. This study within the larger BLSA requires a special cohort of women. While BLSA participants come every 2 years, those who are also in the Perimenopausal Initiative, like Cofield, must be willing and able to visit the GRC every 3 months until they have not had a menstrual period for 2 years. Each visit takes about 3 hours.

In addition, to be eligible for the study, women must be between the ages of 45 and 55, be still menstruating or have had a period in the last 6 months, and have a history of regular periods.

And because this is a study of the "natural" menopause—what bodily changes take place when women are taking no medications—participants cannot be using hormone therapy, birth control pills, or other medicines that might affect the study's findings. The volunteers will be able to take part in a clinical trial of hormone replacement, however, once they have been 24 months without a period.

The special criteria make recruitment difficult. Applications have to be screened carefully, and a lot of potential recruits do not meet all the conditions.

Yet there are advantages to being part of the study that the researchers hope will keep applications coming. Participants receive detailed free information that will help them and their doctors evaluate their risk for osteoporosis and their need for hormone replacement therapy after menopause. "It's a very interesting program," says Jo Ann Lee-Bennett, one of the new recruits. "You learn a lot about your health."

Participants also automatically become lifetime members of the larger study, the BLSA. This longitudinal study on aging is more than 35 years old, and its nearly 1200 volunteers speak enthusiastically about their visits to the BLSA every 2 years.

One advantage they cite is the sense of contributing to scientific advances that can affect them directly. Women, who have been part of the BLSA since 1978, often feel this keenly, since they have been underrepresented in many other studies.

So have African Americans, points out Hiscock. The 100 African American and 100 white women who take part in the Perimenopausal Initiative will supply some of the missing answers about what actually happens during menopause in these two ethnic groups. "So maybe the next generation," says Purnell Cofield, "won't have to hear horror stories."

Caroline McNeil, writer/editor, the National Institute on Aging.

COMPREHENSIVE EFFORT FOCUSES ON

Reducing AIDS Among Minority Drug Users

Data from the National Institute on Drug Abuse (NIDA) show that individuals who inject drugs are changing their AIDS risk behaviors due to effective interventions which NIDA supports in their communities.

Early in the AIDS epidemic, NIDA recognized the link between drug use and the spread of the human immunodeficiency virus (HIV) that causes AIDS. The primary route of HIV transmission in users who inject drugs is sharing needles and using other such injecting devices. Many drug users also place themselves at significant risk by engaging in unprotected sexual behaviors.

In October 1993, the Centers for Disease Control and Prevention (CDC) reported that injection drug users (IDUs) were the second largest group with HIV/AIDS; among both adult and adolescent cases, 24 percent were due to injection drug use, and 3.5 percent to sex with an injection drug user.

Of the 339,250 total AIDS cases, 31 percent were African American, 17 percent were Hispanic, and less than one percent were Asian/Pacific Islander. Of those who injected drugs, 51 percent were African American, 27 percent Hispanic, and less than one percent were Asian/Pacific Islander and other.

During the same period, almost 25,000 cases of AIDS occurred in individuals who reported heterosexual contact as their only risk factor; 50 percent of them admitted to having been sexually involved with a user who injected drugs.

> PRELIMINARY FINDINGS INDICATE THAT INJECTION DRUG USERS ARE HIGHLY CONCERNED ABOUT AIDS, AND WILLING TO MAKE MEANINGFUL CHANGES IN RISK BEHAVIORS.

Despite these alarmingly high rates, AIDS is a preventable disease and, as such, federally-sponsored researchers have been investigating a variety of ways to encourage individuals to change their behavior to reduce the risk of HIV infection.

The purpose of NIDA's programs is to determine the nature and extent of risk-taking behavior; to monitor changes and trends in such behavior in target communities over time; and to assess HIV infection among high-risk populations of injection drug users nationwide, which includes significant numbers of minorities.

Traditionally, most drug users, particularly those not in treatment programs, have been referred to as a "hidden" population difficult to assess for study purposes. To reach them, community-based programs employ local outreach workers, often former drug users themselves, to canvass high drug use areas. The workers hold discussions with individuals on AIDS-related risk behaviors, and distribute prevention materials. Trusting relationships gradually develop, and this "hidden" population becomes accessible to those who are testing the effectiveness of specific interventions. Some of these interventions include voluntary HIV antibody pre- and post-test counseling, and referral to drug treatment or other services.

Research results from NIDA programs indicate that its community-based, street outreach projects have been extremely effective in recruiting individuals, particularly African American and Hispanic IDUs and crack cocaine smokers. They provide information, bleach for cleaning needles which may be HIV-infected, condoms, and confidential HIV antibody testing. The projects have also helped to significantly reduce the sharing of drug paraphernalia, and some high-risk sexual behaviors, and also to encourage those who inject drugs to seek treatment—many of them for the first time.

National AIDS Demonstration Research Project

NIDA's initial program was the National AIDS Demonstration (NADR) Program (1987-1992). Data were collected and studied on substance use patterns among high-risk injection drug users and their sexual partners. The majority of participants recruited for the study were African Americans, Puerto Ricans, Native Americans, and Hispanics at high risk due to their drug use practices and sexual behaviors. The program also evaluated the effectiveness of interventions designed to reduce or eliminate risky behaviors including needle sharing, multiple drug abuse, and unsafe sexual activities.

The projects collected data among users not in treatment and their sexual partners in 61 cities. Enrollees were offered free confidential HIV antibody testing and provided with behavioral counseling including risk reduction methods in a variety of settings—storefronts, mobile vans, church basements.

More than 66,000 injection drug users and their sexual partners were recruited and received baseline risk assessment interviews. More than 22,600 of those initially recruited completed the intervention program, and returned six months later for follow-up (behavior change interview). Of those, African American males were the largest segment—49 percent aged 25 to 44; 13.7 percent were Puerto Ricans, and 13.1 percent other Hispanics.

"The aggregate data from NADR shows considerable effectiveness in reducing HIV-related drug risks," says Dr. Richard Needle, program coordinator and chief of NIDA's Community Research Branch in the Division of Clinical Research.

"Whether there are more culturally sensitive interventions that are selectively better for subgroups of at-risk populations is a question we are currently addressing in the Cooperative Agreement Program," he says.

Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program

Begun in 1990, the AIDS cooperative agreement program builds upon the NADR experience. While the NADR project was effective in helping reduce AIDS risk behaviors, the cooperative agreement program consists of a more rigorous design with modified randomized clinical trials and standard protocols. Seropositivity is monitored of those high-risk street populations who inject drugs and who smoke crack cocaine, in both high- and low-HIV prevalence areas; risk-reduction methods are evaluated. Currently, 21 sites participate in the cooperative agreement program.

Between September 1990 and November 1993, the program had recruited over 13,000 injection drug and crack cocaine users. Of these, 54.1 percent were African Americans; 12.7 percent, Puerto Ricans; 11.3 percent, other Hispanics; and 2.8 percent, Native Americans.

Preliminary findings indicate that injection drug users are highly concerned about AIDS, and willing to make meaningful changes in risk behaviors by cleaning needles and decreasing shared use of injection devices. Says Dr. Needle, "Among the most significant things we have learned is that across and among people of the same gender, race, and ethnicity, there is a remarkable mix of behaviors, so that no single approach will likely be effective if applied across at-risk populations."

New institute research on more targeted HIV prevention programs with subgroups of at-risk populations is already underway.

Karen Rogich, former assistant press officer, the National Institute on Drug Abuse.

Long-Running Programs Increase Number of Minority Scientists

BOTH THE MARC AND MBRS PROGRAMS HAVE HAD SIGNIFICANT IMPACT ON THE DEVELOPMENT OF BIOMEDICAL RESEARCH AND RESEARCH TRAINING CAPABILITY AT MINORITY INSTITUTIONS.

In laboratories from the East coast to the West, graduates of two long-running minority programs are actively contributing to advances in biomedical research. Their accomplishments are the highlights of over 20 successful years for the MARC (Minority Access to Research Careers) and MBRS (Minority Biomedical Research Support) Programs, supported by the National Institute of General Medical Sciences (NIGMS).

A Formula for Success

The success of the MARC and MBRS programs is partly due to their longevity. Many of the schools participating in these programs have been supported since 1972. This continuity of support is critical, because the process of increasing the number of minority biomedical scientists through research and training grants to minority institutions is a long-term investment.

The MARC and MBRS programs grew out of the realization, in the 1960s, that very few federally funded research grants were awarded to science faculty members at colleges and universities with substantial minority enrollments, that most minority Ph.D.s in the current pool are graduates of these institutions, and that the number of minorities with careers in the biomedical sciences was very low.

Because at the time almost 60 percent of minorities who enrolled in graduate school had attended minority institutions as undergraduates, NIH staff members began to study these schools. Visits to a number of HBCUs—historically Black colleges and universities—revealed that a combination of long teaching hours, lack of modern research facilities and equipment, and lack of information about funding sources made it extremely difficult for the faculty to pursue independent research or to introduce their students to up-to-date technology.

Support for the research training of faculty and honors students at minority institutions fits easily into the NIGMS priorities. In 1972, the first two components of the MARC program, the faculty fellowship and visiting scientist awards, were implemented. The MBRS program was launched with grants to 38 institutions in June 1972 by the former NIH Division of Research Resources, which administered MBRS until its transfer to NIGMS in 1989. In addition to NIGMS, most of the other NIH institutes have provided support to the MBRS program by co-funding relevant research subprojects.

The Programs Today

MARC and MBRS are broad, multifaceted programs that provide financial assistance for biomedical research to be conducted, to improve the science education and research environment at minority institutions, and to help students at these institutions enter research careers. The programs are often identified as models for Federal efforts to increase the involvement of underrepresented minorities in scientific research.

The MARC program awards grants to institutions with significant numbers of minority students to provide special science curricula, research training, and support for the research training of faculty members and honors undergraduates. Students in the honors undergraduate program, which began in 1977, are expected to spend a summer or even a semester away from the home institution in a research-intensive laboratory of a major university, national laboratory, research institute, or industrial setting. The MARC program also provides predoctoral fellowships to graduates of the undergraduate program so that they may pursue advanced degrees in the Nation's very best biomedical science graduate programs.

The MBRS Program gives grants to minority institutions to support research projects by faculty members, to provide opportunities for students to work as part of a research team, and to strengthen the institutions' biomedical research capabilities. MBRS also supports enrichment activities and pilot research projects at small undergraduate schools. The enrichment activities include workshops, attendance at scientific meetings, and summer research experiences for faculty and students at off-campus laboratories.

Both the MARC and MBRS programs have had significant impact on the development of biomedical research and research training capability at minority institutions. As a spinoff from this improved research environment, the science curricula at these institutions have been enhanced. The students who participate in these programs, and subsequently seek research careers, serve as role models and set standards of excellence for their institutions. Following are examples of MARC and MBRS successes.

- At the **University of California, Berkeley,** Dr. Wilfred Denetclaw earned his Ph.D. and is currently doing research there on muscular dystrophy. Dr. Denetclaw participated in the MBRS program as an undergraduate at Navajo Community College in Shiprock, NM, and later in the MARC Honors Undergraduate Research Training Program at Fort Lewis College in Durango, CO.
- At **Washington State University** in Pullman, Washington, Dr. Mary Sanchez Lanier, is an assistant professor in the department of microbiology. Dr. Lanier was an MBRS participant both as an undergraduate and graduate student at the University of New Mexico.
- At **Fayetteville State University** in North Carolina, Dr. Matthew Edwards, a former MBRS participant at Howard University in Washington, D.C., is working with a group of scientists at the University of Pittsburgh on studies that will shed light on the physical properties of the cell wall. Dr. Edwards also directs the MBRS program.
- At the **University of California, San Francisco,** Dr. Charles Neal is a fourth-year resident in pediatrics, planning to conduct research in behavioral and developmental pediatrics. He was supported by both the MARC and MBRS programs at the University of California, Santa Cruz, and received the 1991 Medical Scientist Training Program Award at the conclusion of his studies for the M.D.-Ph.D. degree at the University of Michigan Medical School.
- At **Spelman College** in Atlanta, Georgia, Dr. Jann Primus is an assistant professor of biology and conducts research on gene expression at Emory University. Dr. Primus was a MARC honors undergraduate at Spelman College and a MARC predoctoral fellow at the Massachusetts Institute of Technology.
- At the **Massachusetts General Hospital** in Boston, Dr. Mabel Duyao, a former MARC student, helped discover the gene for Huntington's disease. And at the **University of California at Los Angeles,** Dr. Linda Tunstad, a former MARC and MBRS participant, worked in the lab of Nobel Laureate Dr. Donald Cram.

Since the MBRS program began, thousands of student scientists have been introduced to research by working on over 700 different MBRS research projects, and many thousands of scientific papers and posters have been produced by students and faculty at MBRS institutions.

Because of the time required to earn a Ph.D. degree and to conduct postdoctoral research, many graduates of these NIGMS minority programs are just beginning their careers. Each year, new graduates will join them, and the number of minorities in biomedical research will continue to grow.

NIGMS Information Office.

To be eligible for a MARC Honors Undergraduate Research Training Award, applicants must be honor students at a college or university that has a MARC program. The institutions select the students to be supported.

MARC predoctoral awards—and a separate program of predoctoral awards to minority students who were not MARC undergraduates—support graduate training in fields of study that directly prepare students for careers in biomedical research. Areas of study include biology, chemistry, cellular and molecular biology, genetics, biophysics, pharmacological sciences, bioengineering (but not other fields of engineering), and biochemistry.

To be eligible for an MBRS grant, an institution must have a substantial enrollment of minority students. MBRS research grants require the participation of at least 2 faculty members with different research projects. Student research assistants are chosen by the awardee institutions.

For more information, contact:
MARC and MBRS Programs
National Institute of General Medical Sciences
National Institutes of Health
45 Center Dr.
MSC 6200
Rm 2 AS/37
Bethesda, MD 20892-6200
Telephone: (301) 594-3900

Nursing Research Examines Long-Term Care and Aging in Minorities

If we're lucky, we grow old. And more of us are doing just that. Between 1950 and 1980, the elderly population in America doubled from 12.3 million to 25.5 million. By the year 2050, one out of every five persons will be elderly.

Besides growing in size, the elderly population has diversified as the cultural make-up of America has changed. With these changes comes the need to examine how people of different cultural, geographic and economic backgrounds respond to the challenges of aging, and how they move in and out of the health care system as they age.

Nurse researchers are analyzing these challenges, looking for solutions when there are problems. For example, the National Institute of Nursing Research is funding a number of studies that examine long-term care and aging in minorities. Some of the studies were funded in response to the institute's collaborative initiative with the National Institute on Aging; others were investigator-initiated proposals. All of them share a common goal: to understand how various elderly minorities use health care so that ways can be found to improve their care.

Rural Colorado: Connections Flourish Despite Distances

Dr. Joan Magilvy of the University of Colorado School of Nursing recently completed a 4-year study on the use of home health care by the elderly in eight rural Colorado counties, two of which are among the poorest counties in the country. These areas have a high percentage of people over age 60 and include many Hispanics of Spanish descent, as well as Caucasians of European descent.

Magilvy wanted to find out how home health care was provided by area nurses and doctors, as well as how it was received by the counties' elderly residents and their families. Home health care is a whole variety of services which can include basic nursing care, help with bathing or personal care, or housekeeping and shopping.

To gather information about the residents of these rural counties, Magilvy and her research team steeped themselves in their surroundings. "We'd arrive every three to four months and stay for about a week—interviewing, photographing and observing. We also subscribed to the local papers, which kept us in touch with the areas between visits," she said.

The research design, called ethnography, yielded a first-hand description of life in a rural culture through hours of taped interviews and hundreds of photographs, backed by written records and countless team meetings. The research findings both sobered and encouraged Magilvy.

"We found that a significant number of the rural elderly 'fall through the cracks' in the health care system," she explained. "For example, older rural patients who are discharged from urban hospitals may not be informed about home health care. Someone assumes that a family member, usually a daughter, may provide informal care when, in fact, the daughter has six kids and is working outside the home, or she moved away from the area to find a job."

The result of these economic realities is that the elderly—particularly the Hispanic elderly—are getting less "hands-on" home care from family members. In fact, Magilvy found that Hispanics were beginning to enter area nursing homes, which was unheard of only a few years ago.

Despite the unsettling trend of receiving less home care from family members, Magilvy found that the rural elderly—both healthy and frail—felt strongly connected to family, friends, and neighbors who provide a circle of informal support that may include some help with meals and household tasks, transportation, and companionship. Above all, the rural elderly fiercely value their independence and may prefer to rely on this informal network of help rather than formal home care, which some elderly view as "one step away from the nursing home."

According to Magilvy, "This calls for further investigation and some creative problem-solving. Many of these older people live with chronic health problems—problems that most people wouldn't tolerate—because they think formal home care would jeopardize their independence. We need to find a way to get them the care they need while preserving their independence and sense of family."

Illustration by Elizabeth Wolf

Other barriers to receiving home care include restricted eligibility requirements, the long distances nurses and other personnel must travel and the limited number of qualified nurses in rural settings. Nurses also cited their frustration with tedious and complex insurance paperwork, which decreased the time available for home care visits and discouraged some nurses from seeking these positions.

BESIDES GROWING IN SIZE, THE ELDERLY POPULATION HAS DIVERSIFIED AS THE CULTURAL MAKE-UP OF AMERICA HAS CHANGED.

Magilvy is now working on a three-year study that will focus on what happens to rural older adults, particularly the Hispanic population, as they move between health care settings, such as from home care to nursing homes or from hospitals to adult day care. She has added five more counties to the study.

Says Magilvy, "I hope our findings lead to answers that can really make a difference to these older people, including minorities, so that their health and the quality of their lives can be the best possible." She added, "I also hope more attention is paid to these health issues nationwide. If our research findings contribute important knowledge that is applicable to other populations and locations, we will have achieved our goal."

Marianne Glass Duffy, information specialist, the National Institute of Nursing Research.

NATIONWIDE PROGRAM

Educates African Americans About Glaucoma

GLAUCOMA AFFECTS 3 MILLION AMERICANS AND IS THE LEADING CAUSE OF BLINDNESS IN AFRICAN AMERICANS. GLAUCOMA DEVELOPS EARLIER IN AFRICAN AMERICANS THAN IN WHITES AND PROGRESSES MORE RAPIDLY.

Chances are that if you are African American and over age 40, you haven't heard about glaucoma, but you will hear about it soon.

The National Eye Health Education Program (NEHEP), coordinated by the National Eye Institute (NEI), has embarked on a nationwide education program urging African Americans over age 40 and all people over age 60, groups at high risk for the potentially blinding eye disease, to protect their vision by regularly having dilated eye examinations. With early detection and timely treatment, it is possible to control this disease before it steals sight.

The NEHEP launched its public education program after NEI's own scientists and scientist grantees discovered that glaucoma, which often has no early symptoms, had reached near epidemic proportions among middle-aged and older African Americans, particularly men. How researchers discovered the severity of the glaucoma problem in African Americans offers an interesting glimpse into the process whereby biomedical research, in addition to yielding novel new treatments, produces clear public health messages that benefit millions of people. Glaucoma affects 3 million Americans and is the leading cause of blindness in African Americans. It progressively damages the eye's optic nerve, a bundle of nerve fibers that relays visual signals from the eye's retina to the brain. Because glaucoma is associated with increased fluid pressure at the front of the eye, it can often be controlled early on with medications that reduce the pressure. In 1975, while performing an analysis of state blindness registry data, National Eye Institute epidemiologists noticed something alarming:

You could be going blind and not even know it.

That's what glaucoma does. It sneaks up on you – gradually. Glaucoma is a leading cause of blindness among *all* adults over 60.

But it's especially common among African Americans. If you're Black and over 40, you're up to five times more likely to develop it.

Vision loss from glaucoma is permanent. But glaucoma can usually be controlled and the risk of blindness reduced if it's detected and treated early.

So, get a dilated eye examination in which drops are used to enlarge your pupils. This allows your eye care professional to see more of the inside of your eye to check for signs of glaucoma. It doesn't hurt, it's easy, and it could save your eyesight.

For more information about glaucoma, please write National Eye Health Education Program, Box 20/20, Bethesda, MD 20892.

Don't lose sight of glaucoma.

NATIONAL EYE HEALTH EDUCATION PROGRAM

National Eye Institute, National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services

African Americans were eight times more likely to go blind from glaucoma than whites. Although many eye care professionals had noticed that glaucoma was more common in African Americans than whites, few suspected that there was such a large racial difference.

Or was there? The NEI researchers noted that state blindness registries, which depend on the patients themselves reporting their vision problems, tend to understate new cases of blindness. They also wondered if African Americans might just be over-represented in the registries.

Despite these inherent problems, the NEI researchers found no other broad racial disparity for any other cause of blindness listed in the registries. This seemed to support the finding, but again, how reliable were the numbers?

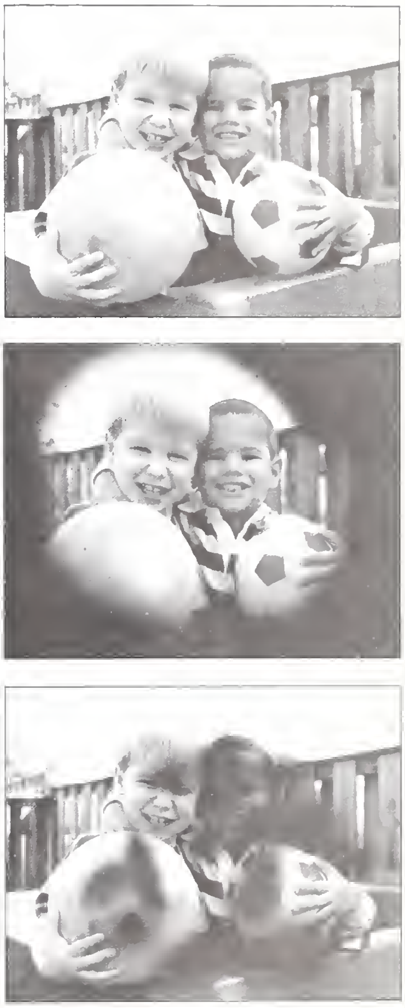
Recognizing the important public health implications involved, the NEI set out to learn more about glaucoma in African Americans. "Regardless of the strengths or weaknesses of the state blindness registry data, this was clearly an area that the NEI had to make one of its research priorities," said NEI director, Carl Kupfer, M.D.

In the 1980s, the institute funded two population-based studies, the Barbados Eye Study in the Caribbean and the Baltimore Eye Survey in the United States. The latter study was particularly important because it was conducted in a racially mixed population using the same rigorous examination criteria for African Americans and whites.

During the late 1980s, the data started to pour in. The Barbados Eye Study showed that 13 percent of African Americans on the island had glaucoma. Another study on the nearby island of St. Lucia reported that 12.2 percent of African American residents had glaucoma.

In July 1991, the Baltimore Eye Survey reported these data:

- African Americans are five times more likely to develop glaucoma than whites.
- Glaucoma develops earlier in African Americans—around age 40—than in whites and progresses more rapidly. By age 70, one in eight African Americans has the disease.



Top: Normal Vision

Middle: The same scene as it might be viewed by a person with glaucoma.

Bottom: The same scene as it might be viewed by a person with diabetic retinopathty.

- Glaucoma is a leading cause of blindness among African Americans.

In fact, African Americans are four times more likely to become blind from the disease than whites.

In December, 1991, the NEI recommended that all people at risk for glaucoma have an eye examination through dilated pupils at least once every two years. It was one of the first Federal recommendations ever issued on eye care.

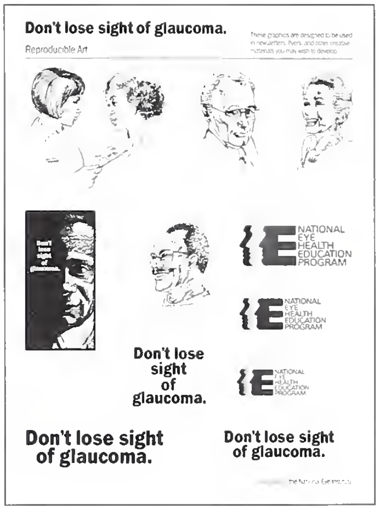
At the same time, the NEI launched the National Eye Health Education Program, a partnership of over 50 public and private organizations, that featured a glaucoma public education program.

The program educates people about glaucoma through several innovative approaches such as:

- Public service announcements on television stations nationwide.
- Community-based eye health education programs.
- A billboard campaign now underway in 14 U.S. cities.

Today, vision researchers continue to investigate the link between glaucoma and African Americans through the NEI-supported Collaborative Initial Glaucoma Treatment Study and other clinical and laboratory investigations. As scientists learn more about this problem and devise more effective methods of treatment, the NEHEP will continue to translate science into improved public health.

Bob Kuska, science writer, the National Eye Institute.



Don't lose sight of glaucoma.

Reproducible Art

These graphics are designed to be used in newsletters, flyers, and other creative materials you may wish to develop.

Don't lose sight of glaucoma.

Don't lose sight of glaucoma.

Don't lose sight of glaucoma.

Don't lose sight of glaucoma.
NATIONAL EYE HEALTH EDUCATION PROGRAM
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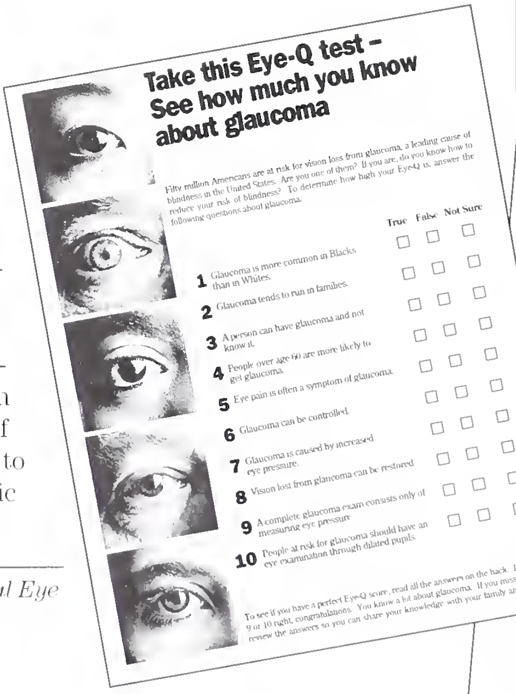
NATIONAL EYE HEALTH EDUCATION PROGRAM

the National Eye Institute

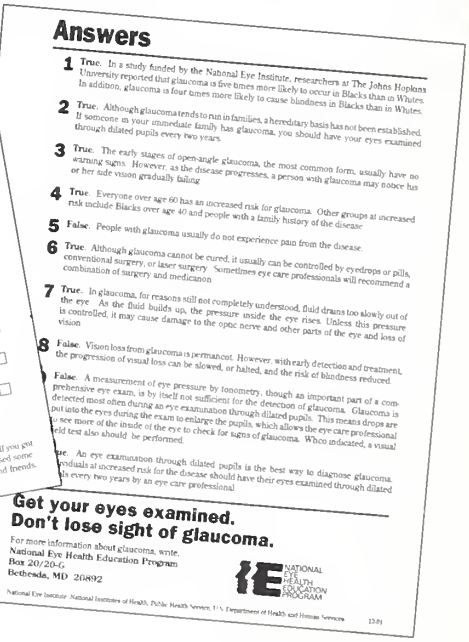


Take this Eye-Q test – See how much you know about glaucoma

Fifty million Americans are at risk for vision loss from glaucoma, a leading cause of blindness in the United States. Are you one of them? If you are, do you know how to reduce your risk of blindness? To determine how high your Eye-Q is, answer the following questions about glaucoma.

		True	False	Not Sure
1	Glaucoma is more common in Blacks than in Whites.	☐	☐	☐
2	Glaucoma tends to run in families.	☐	☐	☐
3	A person can have glaucoma and not know it.	☐	☐	☐
4	People over age 60 are more likely to get glaucoma.	☐	☐	☐
5	Eye pain is often a symptom of glaucoma.	☐	☐	☐
6	Glaucoma can be controlled.	☐	☐	☐
7	Glaucoma is caused by increased eye pressure.	☐	☐	☐
8	Vision lost from glaucoma can be restored.	☐	☐	☐
9	A complete glaucoma exam consists only of measuring eye pressure.	☐	☐	☐
10	People at risk for glaucoma should have an eye examination through dilated pupils.	☐	☐	☐

To see if you have a perfect Eye-Q score, read all the answers on the back. If you got 9 or 10 right, congratulations. You know a lot about glaucoma. If you missed some review the answers so you can share your knowledge with your family and friends.



Answers

1 **True.** In a study funded by the National Eye Institute, researchers at The Johns Hopkins University reported that glaucoma is five times more likely to occur in Blacks than in Whites. In addition, glaucoma is four times more likely to cause blindness in Blacks than in Whites.

2 **True.** Although glaucoma tends to run in families, a hereditary basis has not been established. If someone in your immediate family has glaucoma, you should have your eyes examined through dilated pupils every two years.

3 **True.** The early stages of open-angle glaucoma, the most common form, usually have no warning signs. However, as the disease progresses, a person with glaucoma may notice his or her side vision gradually failing.

4 **True.** Everyone over age 60 has an increased risk for glaucoma. Other groups at increased risk include Blacks over age 40 and people with a family history of the disease.

5 **False.** People with glaucoma usually do not experience pain from the disease.

6 **True.** Although glaucoma cannot be cured, it usually can be controlled by eyedrops or pills, conventional surgery, or laser surgery. Sometimes eye care professionals will recommend a combination of surgery and medication.

7 **True.** In glaucoma, for reasons still not completely understood, fluid drains too slowly out of the eye. As the fluid builds up, the pressure inside the eye rises. Unless this pressure is controlled, it may cause damage to the optic nerve and other parts of the eye and loss of vision.

8 **False.** Vision loss from glaucoma is permanent. However, with early detection and treatment, the progression of visual loss can be slowed, or halted, and the risk of blindness reduced.

False. A measurement of eye pressure by tonometry, though an important part of a comprehensive eye exam, is by itself not sufficient for the detection of glaucoma. Glaucoma is detected most often during an eye examination through dilated pupils. This means drops are put into the eyes during the exam to enlarge the pupils, which allows the eye care professional o see more of the inside of the eye to check for signs of glaucoma. When indicated, a visual eld test also should be performed.

ue. An eye examination through dilated pupils is the best way to diagnose glaucoma. viduals at increased risk for the disease should have their eyes examined through dilated ils every two years by an eye care professional.

Get your eyes examined. Don't lose sight of glaucoma.

For more information about glaucoma, write:
National Eye Health Education Program
Box 20/20-G
Bethesda, MD 20892

National Eye Institute National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services 12-91

VARIOUS MATERIALS, RANGING FROM REPRODUCIBLE ART (TOP) THAT CAN BE USED IN NEWSLETTERS AND OTHER PUBLICATIONS TO BASIC CONSUMER INFORMATION ON GLAUCOMA (BOTTOM) ARE DISTRIBUTED AS PART OF NEI'S PUBLIC EDUCATION CAMPAIGN.

Genes Play Important Role in Minority Drinking Habits

Research sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) has established that certain genes help determine the susceptibility of various minority groups to alcohol abuse. Results of this research may suggest interventions for preventing alcohol abuse and its consequences.

Ting-Kai Li, M.D., of Indiana University School of Medicine, has conducted research in this area under NIAAA sponsorship. "A large segment of the world population—including Chinese, Japanese, Koreans, and possibly some others—are protected against heavy drinking to some extent," Dr. Li said. "This protection is conferred by an unpleasant 'flushing' reaction that occurs when they drink even small quantities of alcohol." The flushing reaction produces such unpleasant symptoms as hot skin, increased heart rate, dizziness, and nausea.

Flushing reaction has been traced to the inheritance of a defective gene for alcohol metabolism. Alcohol is generally metabolized (broken down) by two enzymes. Alcohol dehydrogenase (ADH) converts alcohol to acetaldehyde, a chemical potentially more toxic than alcohol itself. A second enzyme, aldehyde dehydrogenase (ALDH), then detoxifies the acetaldehyde. The gene that is defective in alcohol-flushers produces an inactive form of ALDH, causing the toxic acetaldehyde to build up in the body when alcohol is consumed. Fifty percent of Chinese and Japanese populations are believed to have the defective gene.

The presence or absence of defective ALDH may also help predict the prevalence of alcohol-related health consequences in some minority groups. In NIAAA-sponsored research, Akitaka Shibuya and Akira Yoshida determined that Japanese subjects with the defective ALDH gene are at a much lower risk for developing alcoholic liver disease than are those with the normal gene. The researchers suggest that flushers are deterred from drinking sufficient alcohol over the years to develop liver disease.

> THE DEMONSTRATION OF SPECIFIC GENES THAT INFLUENCE DRINKING BEHAVIOR IS A MAJOR ADVANCE IN THE STUDY OF ALCOHOLISM.

The demonstration of specific genes that influence drinking behavior is a major advance in the study of alcoholism. However, different forms of alcohol metabolizing enzymes are only one of the many genetic factors that influence drinking behavior. Environmental factors also influence alcohol consumption, and may alter or override the effect of the genetic factors. For example, many Asians who experience the flushing reaction continue to drink, and recent studies have reported that alcohol consumption is increasing among Asians as a result of social and environmental factors.

One such study showed that a group of Chinese immigrants in North America changed their drinking practices as they became acculturated. Initially, drinking was significantly less common among those who were ALDH-deficient. Over three generations, drinking increased in both the normal-ALDH and defective-ALDH populations, although the increase was slower in the ALDH-deficient group. These findings suggest that future studies will need to observe closely the biological and psychosocial factors that influence drinking behavior.

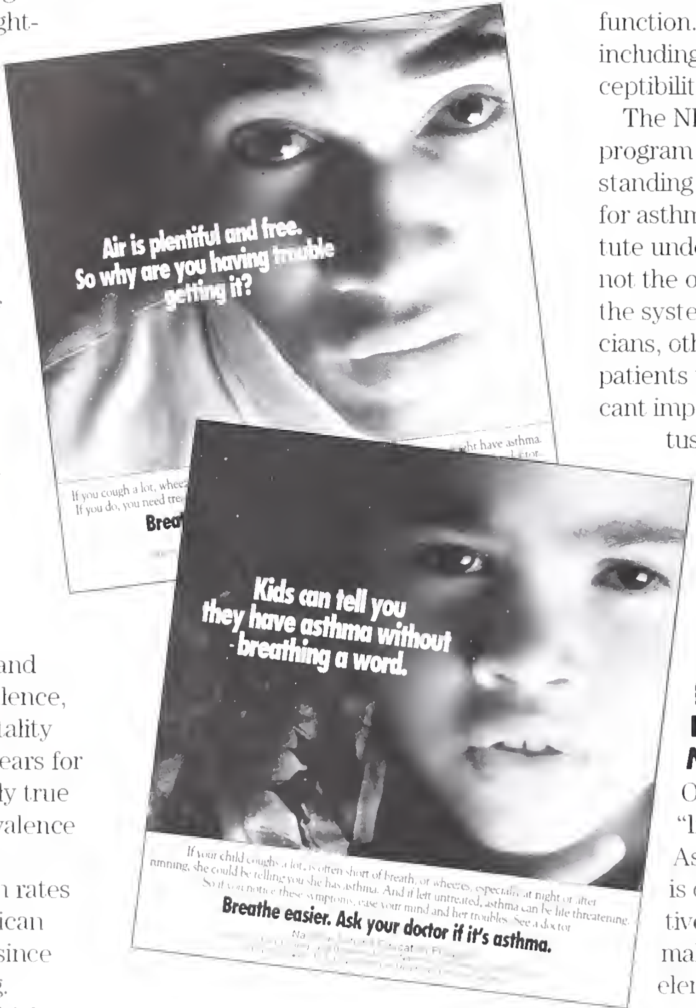
The results of alcohol metabolism studies have relevance for alcoholism treatment research. One treatment goal, Dr. Li said, is "the development of medications to reduce the craving for alcohol in people who drink despite belonging to a population genetically protected from alcoholism. In addition, we must develop and apply treatment measures appropriate to groups that do not have this genetic protection."

Diane Miller, information officer, the National Institute on Alcohol Abuse and Alcoholism.

RESEARCH AND EDUCATION COMBINE TO

Prevent and Cure Asthma Among African Americans

Coughing. Wheezing. Shortness of breath. Tightness in the chest. These are major warning signs of asthma, and they're being highlighted in a new mass media campaign developed by the National Heart, Lung, and Blood Institute (NHLBI). The campaign is targeted at people with asthma symptoms who are not in treatment, especially African Americans. It has been designed to make them aware of the potential severity of asthma and to encourage them to seek treatment. The ultimate aim — to prevent and control asthma symptoms through better detection and treatment.


Air is plentiful and free.
So why are you having trouble getting it?
If you cough a lot, whee
If you do, you need tre
Brea
ght have asthma.
Kids can tell you they have asthma without breathing a word.
If your child coughs a lot, is often short of breath, or wheezes, especially at night or after running, she could be telling you she has asthma. And if left untreated, asthma can be life threatening. So if you notice these symptoms, ease your mind and her troubles. See a doctor
Breathe easier. Ask your doctor if it's asthma.

Asthma Cases Higher, More Serious Among African Americans

Despite advances in research and improved therapy, asthma prevalence, severity, and morbidity and mortality have been increasing in recent years for all Americans. This is particularly true for African Americans. The prevalence of asthma is higher in African Americans than in whites. Death rates for asthma also are higher in African Americans than in whites. And since 1950, the gap has been widening. Asthma mortality is three times higher in African American men and two times higher in African American women than in white men and women, respectively.

Many reasons have been advanced to explain why the burden of asthma is falling so heavily on African Americans. Some relate to socioeconomic status — for example, lack of access to care, or greater exposure to environmental factors that trigger asthma symptoms like cockroaches and dust mites, or higher incidence of low birth-weight infants with poorly developed lung function. Others are more general, including the possibility of genetic susceptibilities.

The NHLBI expects its basic research program will soon yield a better understanding of the causes and risk factors for asthma. At the same time, the institute understands that basic research is not the only answer. In fact, improving the system of care and educating physicians, other health care providers, and patients themselves will result in significant improvements in their health status. To this end, the institute is supporting a number of initiatives to develop model education programs with a special emphasis on preventing and controlling asthma among minority populations.

A NUMBER OF MODEL EDUCATION PROGRAMS EMPHASIZE PREVENTING ASTHMA AMONG MINORITIES.

Intervention Programs Reach Out to Minorities

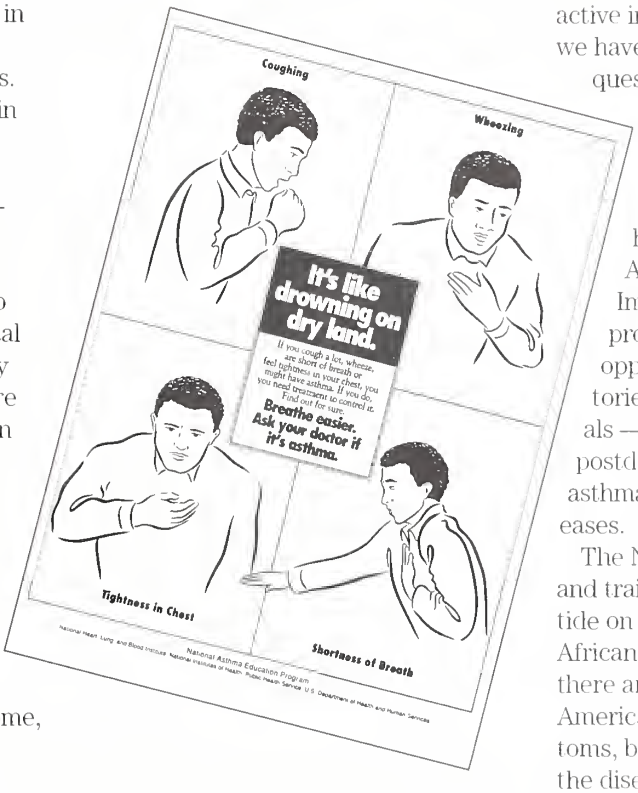
One new NHLBI initiative, "Interventions to Improve Asthma Management at School," is designed to stimulate innovative programs for ensuring optimal asthma management among elementary and junior high school students in inner-city or rural schools with high proportions of minority students. These model programs are expected to identify cost-effective mechanisms for improving identification and referral of children with uncontrolled asthma; for increasing participation of students with asthma in all school activities, including physical education and sports; for ensuring that students with asthma have appropriate access to their medications; and for improving communication between school and home.

Similarly, NHLBI's "Interventions to Control Asthma Among African American and Hispanic Children" is supporting 5 model projects that are testing new organizational approaches to improve medical care, monitor children's asthma, and educate families in asthma management in African American and Hispanic communities. For example, at Howard University in Washington, D.C., researchers are investigating the effectiveness of a school- and a community-based outreach program to assist African American children with asthma.

In New York City, under a grant to Columbia University, 11 experimental child health clinics, which previously had provided only well-baby care, are now aggressively identifying children with asthma, providing up-to-date medications and intensive patient education. And researchers at Washington University in St. Louis, in collaboration with a private social welfare agency, are organizing and evaluating a neighborhood support program for improving asthma management in low-income, mostly African American children.

One of the institute's minority grantees, Dr. Floyd J. Malveaux, argues that these types of interventions, by emphasizing disease prevention and health promotion, can help reduce the high cost of providing asthma care.

ASTHMA MORTALITY IS THREE TIMES HIGHER IN AFRICAN AMERICAN MEN AND TWO TIMES HIGHER IN AFRICAN AMERICAN WOMEN THAN IN WHITE MEN AND WOMEN, RESPECTIVELY.


Coughing
Wheezing
It's like drowning on dry land.
Breathe easier. Ask your doctor if it's asthma.
Tightness in Chest
Shortness of Breath
National Asthma Education Program
National Heart, Lung, and Blood Institute National Institutes of Health Public Health Service U.S. Department of Health and Human Services

If you cough a lot, wheeze, are short of breath or feel tightness in your chest, you might have asthma. If you do, you need treatment to control it. Find out for sure.

EDUCATION MATERIALS DESCRIBE THE WARNING SIGNS OF ASTHMA.

Future Progress Depends on More Minority Researchers

Chairman of the Microbiology Department at the Howard University College of Medicine, Dr. Malveaux emphasizes that increasing the number of basic and clinical researchers from minority backgrounds is critical to addressing the high rates of asthma morbidity and mortality in minority communities. "We need to make a concerted effort to attract more minorities into fields where they can become active in investigation — to make sure we have people who can ask the right questions and get good answers."

That concerted effort has already begun. The NHLBI and the National Institute of Allergy and Infectious Diseases have joined with the American Academy of Allergy and Immunology (AAAI) in a special program to provide research opportunities in established laboratories and to train minority individuals — from the high school through postdoctoral levels — in the field of asthma, allergy and immunologic diseases.

The NHLBI hopes that these research and training activities will soon turn the tide on the tragedy of asthma among African Americans. In the meantime, there are an estimated 12-25 million Americans who may have asthma symptoms, but many do not know they have the disease until they suffer an acute attack. That's what the institute's mass media campaign seeks to change. It promotes the warning signs of asthma and tells the African American audience it is targeting, "Breathe easier. Ask your doctor if it's asthma."

Louise Williams, public affairs specialist, the National Heart, Lung, and Blood Institute.

B
H

Nurse Researchers Study Ways to Improve Outcomes for Pregnant Minority Women

Every year, nearly 30,000 American babies die because they are born too early and don't weigh enough at birth. Those that live may have chronic disabilities such as cerebral palsy, blindness, or mental retardation. Add to this the tremendous financial burden of intensive care hospitalization, and the tragedy of America's high rate of low-birthweight is all too clear.

With often very limited access to health care, minority groups are at particular risk for low-birthweight babies. But access isn't everything. Through nursing research, other factors such as cultural beliefs and social support are emerging as important influences on the health of pregnant minority women and their babies.

Recognizing low birthweight as a research priority, the National Institute of Nursing Research is funding a variety of studies examining the factors behind this problem and testing interventions—some based on societal and cultural factors—to increase the number of healthy, full-term babies.

Regular Phone Calls Making Healthier Babies

"Babies have always been a special interest of mine," says Dr. Mary Lou Moore, of the Bowman Gray School of Medicine. What started as a personal interest became a career and, over time, Moore shifted her focus from general pediatrics to research on the prevention of pre-term and low-birthweight babies.

> WITH OFTEN VERY LIMITED ACCESS TO HEALTH CARE, MINORITY GROUPS ARE AT PARTICULAR RISK FOR LOW-BIRTHWEIGHT BABIES.

Several years ago, when Moore read a study showing that premature labor was detected just as well by regular phone calls from a nurse to women at home as by expensive home fetal monitors, her interest was fueled. In 1990, she devised her own research focusing on women at risk for low birthweight—African American women, all teenagers, and white women who were identified as at-risk for low-birthweight births.

Moore divides her subjects into two groups, both of which receive routine prenatal care. One group of women, however, also receives telephone calls from a nurse two to four times a week during the last 12 weeks of pregnancy. The nurse reminds each patient to eat healthy foods and take vitamins, and asks about any unusual symptoms like pains or cramping, sometimes signs of pre-term labor. Ways to deal with the symptoms, ranging from bedrest and increased fluids to hospitalization, are discussed.

Preliminary results from the 5-year study show that low-birthweight births were reduced one-third in the group receiving phone calls. Though perhaps not high-tech, this innovative approach appears to be effective and inexpensive.

The nurses wear beepers, and so are easily accessible

This close, reliable contact "may be the most support these women have, especially those used to seeing a different doctor every time they visit the public clinic," says Moore. "Since 85 percent of the women are single, the nurses are filling a void—and they are always available."

Moore is currently collecting cost data, but common sense tells her that this intervention is fairly cost-effective. "If no one is home when the nurse calls, she's wasted about one minute of time. And the beepers are downright cheap compared with an $80-a-day home fetal monitor," she says.

The next step will be to study these mothers and their children to age 3, looking at outcomes such as immunizations, developmental milestones, and the mothers' plans for education and family planning. "The women who deliver at term see it as a personal success, which takes hold in other areas of their lives," says Moore. They start planning their lives—many for the first time—and taking initial steps to reach their personal and family goals."

Culturally-Sensitive Prenatal Care: Patients As Experts

Dr. Dyanne Affonso speaks with passion and precision about America's poor marks in preventing infant mortality and low-birthweight babies. "One reason we haven't been successful is because prenatal care is not supported by cultural practices for the women who remain outside the health care system."

Affonso, Dean of Emory University's School of Nursing, is out to change that, starting with her native corner of the world, Hawaii. She's heading a 5-year study funded by the National Institute of Nursing Research to develop a model of culturally sensitive, community-based prenatal care services. Known as "Malama Na Wahine Hapai" or "Caring for Pregnant Women," the project focuses on Hawaiian, Filipino, and Japanese women living in the rural areas of Hilo and Puna on the island of Hawaii. These women historically have had higher rates of low-birthweight babies.

Affonso's first challenge was to learn why. She spent months interviewing women from the three ethnic groups, and learned many things not found on patient information forms. For instance, she found that Filipinos often don't seek prenatal care because many are embarrassed about their poor English, and that Hawaiians are apt to be more attentive to their present situations than to worry about future circumstances. The Japanese women were particularly puzzling because they came faithfully to standard obstetrical prenatal visits, yet their low-birthweight rates were comparable to that of the Filipinos.

All of the women said that, due to time constraints and a perceived lack of sensitivity to their cultures, they were unable to bring their full health care concerns to the attention of providers.

Another common thread among these different cultures is the importance of the women's family and friends for support in their daily lives. Affonso believes that this is the key to creating culturally-relevant prenatal care. "We can improve this care by creating a partnership with the community," she says. "By using the interpersonal support systems that have been in place for years to assist pregnant women, perhaps they will find meaning and self-esteem in being pregnant and improve their health behavior."

ETHNIC HEALER, AUNTIE MARGARET MOCHADO, PERFORMS THERAPEUTIC MASSAGE ON JUNE SHIBUYA, MALAMA PROJECT COORDINATOR.

Affonso is using a number of innovative approaches to reach out to women in their communities. She started a neighborhood women's health watch network, in which local women help to identify pregnant women and encourage them to seek early prenatal care.

Each woman in the program is seen 18 times from beginning pregnancy (6-10 weeks) through the postpartum period. Every visit has a specific theme or purpose that includes providing information and building self-esteem. Knowing that some women are reluctant to travel long distances to unfamiliar clinic settings, Affonso has provided mobile van clinics to bring care to places where rural women gather.

Coordinated through the State Department of Health public health nursing branch, the project seems to involve in some way nearly everyone on this rural island. Affonso has established a community advisory board of representatives from the business community, the mayor's office, and ethnic healers—an important local cultural resource—to help assure that the project remains relevant to the community. Even several men's clubs, such as the Kiwanis, have held celebration parties for the women who have completed the program, she says.

Under Affonso's orchestration, this rural community is engaged in an innovative nursing intervention. Through observation and data measurement, she hopes to duplicate what works here in other communities. Affonso: "By listening to the real experts—the women and the community—we know we can make a difference in the babies' and mothers' health."

Marianne Glass Duffy, information specialist, the National Institute of Nursing Research.

MINORITY WOMEN:

Focus of Research Studies on Obesity

THE ANSWER TO DECREASING OBESITY IN MINORITY WOMEN IS ASSOCIATED WITH CHANGING CULTURAL BELIEFS AND PRACTICES IN COOKING AND EATING.

Estimated to affect as much as one-third of the adult U.S. population, obesity is even more common in African American and Mexican American women. Among them, prevalence of the disease approaches 50 percent. Like other obese individuals, these women have increased risk for diabetes, heart disease, stroke, high blood pressure, gallbladder disease, and some forms of cancer.

In an effort to alleviate the increasing problem of obesity in minority women, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is collaborating with the Office of Research on Women's Health, and the Office of Research on Minority Health to develop treatment programs specifically designed for this high-risk population. These joint research efforts include evaluation of a food-based versus a self-management treatment, and a clinical trial on the long-term outcome of obesity treatment in non-white women. Food-based treatment focuses on changing eating and exercise habits without strict dieting, and a self-management treatment applies behavior modification techniques to control eating.

Despite extensive studies, there is scant evidence that standard treatments of obesity using calorie-restricted diets have much effect on long-term weight loss. Low calorie diets can lead to weight loss over the short term, but most studies show that the majority of participants eventually regain most or all of their lost weight. Rather, the answer to decreasing obesity in minority women particularly is associated with changing cultural beliefs and practices in cooking and eating. These habits and beliefs are often learned in childhood and are difficult to change.

To explore the benefits of an obesity treatment based on eating correctly, exercising, and avoiding strenuous dieting, NIDDK is conducting a 6-month trial of approximately 240 moderately obese African, Mexican, Hispanic, and Asian American women ages 25 to 50. These women are randomized to a food-based treatment group, a self-managed treatment group, or a control group given an appropriate diet without other interventions. Participants in both treatment groups follow a 1000 to 1500 calorie-a-day eating plan based on the U.S. Dietary Guidelines for Healthy Americans.

Six Steps to Better Self Care

Participants in the food-based group follow a six-step approach designed to stop self-destructive cycles of dieting and to ease the psychological strain of being obese. The focus of this approach is to make healthier food choices.

Step one encourages the women to stop dieting. To curb cravings, the women eat three meals a day, with two between-meal snacks. Researchers believe that sensible eating spread out over the day stabilizes blood sugar so that hunger never becomes a problem.

The second step aims at reducing fat to about 30 percent of calories, and asking them to keep a food diary to monitor consumption and to eat from the basic food groups.

Nerve conduction study to measure energy metabolism.

The third step requires participants to reexamine their feelings about food and their weight. By keeping a food and exercise diary, participants monitor what and why they eat. Some eat for social or emotional reasons rather than from hunger. Participants are encouraged to satisfy their body's energy needs by eating regularly and to take time to think through situations when they have cravings for reasons other than hunger. Group leaders help them change their attitudes toward obesity in several ways. They are encouraged to lose fat to promote health instead of cosmetic beauty, join organizations such as the National Association for the Advancement of Fat Acceptance to fight society's prejudices against the obese, to accept the weight they attain with sensible eating and regular exercise, and to place less emphasis on being thin.

Exercise is the fourth step. A brisk 45 minute walk, four to five times a week is recommended. Participants also attend weekly support group meetings, a critical fifth step to the food-based approach. The final step for them is to accept the weight attained with prudent eating and exercise habits.

In the self-managed treatment group, participants learn to consciously limit their eating to a 1000 to 1500 calorie-a-day diet. Interventions focus on developing behaviors that help restrict caloric intake and control stimuli that trigger eating.

While self-managed obesity treatments help other obese people reduce weight, they seem to be less effective for minority women. Research suggests that traditional restrictive diets may be less effective in this high-risk population because such treatments fail to incorporate the attitudes and beliefs of this population. Supplemental funding from the Office of Research on Women's Health enabled the study to include non-white, obese binge eaters, a very difficult group to recruit.

Preliminary results show that women using both treatments lost significant weight, compared to women in the control group. The episodes of binge eating were also lower. Yet to be determined is whether or not these women benefit more from an obesity treatment that is food-based versus one that is self-managed. Final data are expected to be published later this year.

Long-Term Health Outcomes of Obesity Under Study

Also under way is a study designed to investigate the long-term outcome of obesity in 600 African American women. This randomized clinical trial aims to produce a 5 to 10 percent weight loss in obese African American women ages 40 to 64. Its secondary objective is to monitor changes in risk factors for disease such as fasting insulin levels and lipid levels.

The women are randomized to a control group on a 2000 calorie-a-day diet, a food-based group, or a meal replacement group that substitutes two milk-based diet shakes instead of meals.

Those in the food-based and meal replacement groups attend weekly one-hour sessions led by an African American health professional to motivate them to set culturally appropriate short and long-term goals, such as losing weight so that one could care for grandchildren and watch them grow up. Emphasis is also placed on use of ethnic foods that are low in fat, such as sweet potato pie and plantains.

The researchers seek to show that African American women assigned to a culturally specific weight control program will reduce their body weight by 5 to 10 percent compared to a control group, and that this weight loss will be maintained for at least one year.

The hope is that these and other research initiatives ultimately will provide specific models of ethnically appropriate weight loss programs that can be applied to lower the obesity rate in high-risk populations.

Leslie Curtis, writer/editor, the National Institute of Diabetes and Digestive and Kidney Diseases.

Research Centers Established to Improve Minority Oral Health

Illustration by Becky Heavner

Americans as a whole have enjoyed remarkable gains in oral health over the past several decades. Children today have far less tooth decay than their parents and grandparents had as youngsters, and working-age adults are keeping their natural teeth longer. Thirty years ago, 64 percent of adults ages 35-64 were toothless as compared to 26 percent today. These improvements in dental health are mostly the result of advances in disease prevention and treatment.

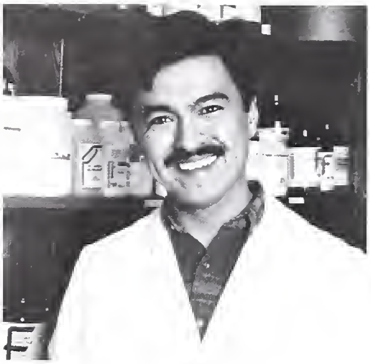
Unfortunately, not everyone in this country has enjoyed similar gains in oral health. This is particularly true of minority populations, who remain at high risk of tooth decay, periodontal (gum) diseases, and other conditions affecting the mouth, face, and jaws.

In the fall of 1992, the National Institute of Dental Research (NIDR) began a new program aimed at improving the oral health of minority populations. The institute awarded developmental grants to help establish Regional Research Centers for Minority Oral Health (RRCMOH) across the country.

MINORITY POPULATIONS REMAIN AT HIGH RISK OF TOOTH DECAY, PERIODONTAL DISEASES AND OTHER DENTAL CONDITIONS.

The first phase of the program consists of developmental grants awarded to six consortia, each with minority dental schools or schools serving minority populations and one school conducting research–intensive oral health programs. Faculty development is a key feature at all the centers, and is designed to increase the number of minority oral health researchers. This particular activity is co-funded by NIH's National Center for Research Resources. In addition, the centers are developing organizational alliances to help strengthen the research capability of those institutions which serve large minority populations. The developmental grants will give these institutions an opportunity to acquire the expertise to compete for the second phase of the program, which consists of 5-year center grants to be awarded in 1995.

Newark, New Jersey. The Newark-based University of Medicine and Dentistry of New Jersey (UMDNJ) is collaborating with the University of Connecticut School of Dental Medicine. Scientists are looking at the effects



Minority dental students receive research training during the summer in a collaborative program sponsored by the National Institute of Dental research (NIDR), the University of Rochester, and industry. The NIDR-university-industry alliance enables these students to benefit from a unique situation in which NIDR provides their stipends, industry provides travel expenses, and the University of Rochester provides housing and training. This joint effort, begun in 1987, has resulted in a model program that encourages minority students to pursue careers in biomedical research.

of heredity, diet, and socioeconomic conditions on the development of dental caries in pre-school children. The researchers will develop preventive programs for those at risk. Other investigators are examining the prevalence and severity of oral lesions in children who were born HIV-positive. A third group of scientists seeks to determine the possible genetic and environmental risk factors associated with oral cancer in African Americans. Dr. Frank Catalanotto, center director, evaluates progress. "The first 15 months have been enormously successful in terms of research and minority faculty development," he says. "Moreover, the center has attracted some complementary funding from other schools at the university, and the university foundation is coordinating a fund-raising effort."

San Antonio, Texas. The University of Texas Health Sciences Center Dental School is collaborating with St. Mary's University, also of San Antonio, and several other academic and community health entities in the southwest Texas region to determine which factors influence the oral health of Mexican Americans. The scientists seek to define the oral health status of residents in the Texas/Mexico border areas, and to study attitudes about the important of oral disease prevention. Another study will examine the effects of nutrition on the oral health of Mexican Americans with noninsulin-dependent diabetes.

New York City, New York. The New York University College of Dentistry and the Forsyth Dental Center in Boston are working together on a number of oral health issues aimed at the diverse minority populations of the City. The primary projects are focusing on the status of oral health and treatment needs of New York's Asian American community. They also are assessing the risk factors for periodontal diseases among African Americans, Hispanics, and Asian Americans.

Nashville, Tennessee. Meharry Dental College is working with the University of Alabama's School of Dentistry in Birmingham to carry out basic studies of connective tissue and oral microbiology. One feature of the grant is to establish a new oral microbiology laboratory at Meharry where faculty researchers will study dental caries in African American infants and children, and devise measures for preventing mother-to-child transmission of decay-causing bacteria.

Los Angeles, California. The UCLA School of Dentistry is collaborating with the Charles R. Drew University of Medicine and Sciences in Los Angeles to study the oral health of African American, Asian American and Hispanic populations. Research teams are investigating new techniques for treating mouth and jaw injuries, measuring both the oral and general health of minorities, and determining the social barriers that prevent minorities from receiving dental care.

Baltimore, Maryland. The dental schools at the University of Maryland, Virginia Commonwealth University, and Howard University have joined together to study oral cancer, periodontal diseases, AIDS, and the general oral health needs of African American children and adults. According to Dr. Harold B. Martin, program director at Howard University, "The alliance has brought together faculty and community leaders with the common goal of improving the oral health of minority communities."

While aiming to improve oral health in minorities, another major goal of the Regional Research Centers initiative is to overcome institutional and cultural barriers that have prevented minority access to oral health care. The catalyst for change are the alliances called for in the initiative between minority dental schools or dental schools serving large minority populations and the established research institutions.

"It is exciting to see this program come to life," says Dr. Harald Loe, former NIDR director and innovator of the concept. "The initiative has energized the research community, both in the minority and the majority schools, and the idea of similar alliances between these schools might extend well beyond the area of oral health," he says. "The consortia approach could be used to address any disease that disproportionately strikes minorities."

Wayne Little, technical writer/editor, the National Institute of Dental Research.

Minority Researchers Are Making A Difference

The following researchers are just a few of the minority scientists supported by the National Institute of Mental Health. They are distinguished by their dedication to improving the mental health of minorities and to training young researchers.

Glorisa Canino, Ph.D., returned home to Puerto Rico in the late 1970s with her doctorate in psychology from Temple University in Philadelphia and planned to be a family therapist. But her first employer - the island's mental health commissioner - insisted Puerto Rico would be best served if Dr. Canino did research instead. "The commissioner insisted that what he needed was incidence data so he could plan services," Dr. Canino recalled. NIMH provided technical assistance and funding for the first of several studies of mental illness prevalence, co-morbidity, and risk factors important in the development of services for people with mental and addictive disorders. Dr. Canino's research findings were key to two Puerto Rican legislature decisions to double mental health funding (1989), and to bring services for alcohol disorders under the mental health commissioner (1992). Nearly two decades and five mental health commissioners later, Dr. Canino still serves as a consultant to the Mental Health Secretariat of Puerto Rico. She is a professor at the School of Medicine, where she directs the Behavioral Sciences Research Institute and helps train young researchers.

Glorisa Canino, Ph.D.

Drawing on what she has learned from more than a decade of research about behavioral, cultural, ethnic, and gender differences, **Gail Elizabeth Wyatt, Ph.D.,** says her goal is to develop interventions for women that are "reality-based and socially appropriate." Dr. Wyatt, professor of medical psychology at the University of California Los Angeles, says she believes many efforts to improve women's health fail because intervention programs are based on models designed for men, or on antiquated data that were never intended to apply to current issues. "You can't treat women like men. It's important to do the research first," said Dr. Wyatt, who is conducting studies on behavior and AIDS in women. The first African American woman to be licensed as a psychologist in California, Dr. Wyatt has been an NIMH Research Scientist Career Development awardee for the past 12 years. She has written numerous articles and two books on sociocultural issues in the psychiatric treatment of ethnic minority children and adults, the lasting effects of child abuse, and how consensual and abusive sexual relationships affect the well-being of African American and Caucasian women.

Gail E. Wyatt, Ph.D.

As a student **Keh-Ming Lin, M.D.,** was interested in human behavior, the humanities, and biology, so when he had to make a decision about a specialty near the end of medical school courses, "It had to be psychiatry," he says. Two decades later, he directs the Harbor-UCLA Research Center on the Psychobiology of Ethnicity, funded by NIMH. Studies focus on the diagnosis and treatment of mental disorders in Asian Americans and how medications are metabolized. "Too often we tend to apply what we know from information and experiences in the majority population,"

Keh-Ming Lin, M.D.

said Dr. Lin, who is a professor of psychiatry at UCLA School of Medicine. "We need to systematically look at differences and how they may apply." Dr. Lin has published numerous scientific articles on behavior and possible cultural factors in psychopharmocology and mental disorders. He also participated in a collaborative research effort to examine the role culture may play in mental illness for the next edition of the Diagnostic and Statistical Manual. The American Psychiatric Association manual is used worldwide by psychiatric clinicians and researchers to classify mental disorders.

James S. Jackson, Ph.D.

James S. Jackson, Ph.D., who directs the Program for Research on African Americans at the University of Michigan's Institute for Social Research, insists he is not a role model. However, he ranks "outreach programs with young people" high on his priority list and says, "I do what I can to help." Pointing to high dropout rates and universal problems with drugs and alcohol abuse, Jackson says success in reaching today's young people depends upon "changing their expectations and letting them know that other things are possible." Jackson, a psychologist and mentor to his peers as well as minority student scientists, began his own career with an early interest in science. Concerns about social and environmental problems and how they influence mental health and mental illness grew while he was working as a probation counselor. As professor of health behavior and education, he is able to use the university medical school's treatment facilities to translate research findings into improved programs and policies for mental health care delivery.

Spero Manson, Ph.D.

It's not health and medicine, but what people say about it that intrigues medical anthropologist and psychologist, **Spero Manson, Ph.D.** A professor in the Psychiatry Department and director of the National Center for American Indian and Alaska Native Mental Health Research at the University of Colorado Health Sciences Center, Dr. Manson says his interest began with his own family. "I would hear the stories they told each other about their health problems, but they didn't think it was appropriate to talk to a physician," he recalled. Learning how social, cultural, and psychological factors affect people's health concerns and the way they address them continues to be a priority for Dr. Manson, whose articles on the assessment, epidemiology, and prevention of alcohol and drug addictions, and mental disorders, have been published extensively. He also serves as editor of a journal dedicated to these concerns among Native Americans and Native Alaskans. In addition to his work at the university center, Dr. Manson also helps direct a privately-funded multimillion dollar project to assist Native American and Native Alaskan communities deal with drug abuse. He is concerned that so few Native Americans have been attracted to careers in mental health. "We need to correct the misconceptions about mental health and convey that to our young people at an early age," Dr. Manson says.

Marilyn Weeks, science writer, the National Institute of Mental Health.

Student Programs Encourage Future Minority Scientists to Study Neuroscience

THE PROGRAM ENABLES STUDENTS TO ACQUIRE BASIC SCIENTIFIC SKILLS AND LEARN HOW THESE SKILLS CAN BE APPLIED TO REAL PROBLEMS.

Each year, for nine years, the National Institute of Neurological Disorders and Stroke (NINDS) has offered hundreds of high school, undergraduate, graduate, and medical school students the opportunity to conduct hands-on research with leading neuroscientists through the Summer Program in the Neurological Sciences.

This pioneering program, which recruits and trains academically talented youth, especially women and minorities, for neuroscience research, was started in 1984 out of a growing concern that America's supply of researchers in the field of neurology was waning. The alarming trend–particularly pronounced among women and minorities–was especially troubling to the NINDS, whose efforts to conduct and support neurological research would be seriously hampered without a new generation of scientists. The institute decided to build a core of young researchers for the future, and thus, the summer program was established.

To be included in the program, students are first selected by NINDS laboratory and branch chiefs who review applications, letters of recommendation and academic records. The students are then assigned to a mentor and given a project in one of the institute's laboratories or clinical branches. The projects usually involve the students in everything from learning fundamental laboratory techniques to conducting technical laboratory experiments.

The summer students come from as far away as California and Puerto Rico and represent many of the country's leading academic institutions, including NINDS grantee institutions.

Currently, there are more than 600 graduates of the program who are now training for careers in biomedical research or academic medicine at such prestigious institutions as Harvard, Stanford, and The Johns Hopkins Universities.

"The program provided me with exposure to basic research that I had not had the opportunity to experience even while in medical school. It helped me to decide to go into research in the neurosciences and to pursue a specialty in neurology," said Dr. Laroy Penix, one of the more than 100 minority graduates of the program.

Last year's class was one of the largest in the program's history. Of the 260 students who applied, 126 were accepted, including 60 minorities. The number of students accepted into the program grows each year.

Dr. Penix, who participated in the summer program when he was a medical student at The Johns Hopkins Medical School "many years ago," as he described it, is now a senior staff fellow in the NINDS Epilepsy Research Branch. He is currently investigating the possible role of nitric oxide in contributing to brain damage during prolonged epileptic seizures. "By coming here (to the NIH) a student can become aware of many different areas of research that he or she otherwise would not be able to," he said. "It's a unique experience."

Recently, the NINDS established the Adopt-A-School program, to introduce potential young scientists to the field of biomedical research, particularly in the neurological sciences. The NINDS adopts local Washington-area high schools with large minority enrollments to help train minority students.

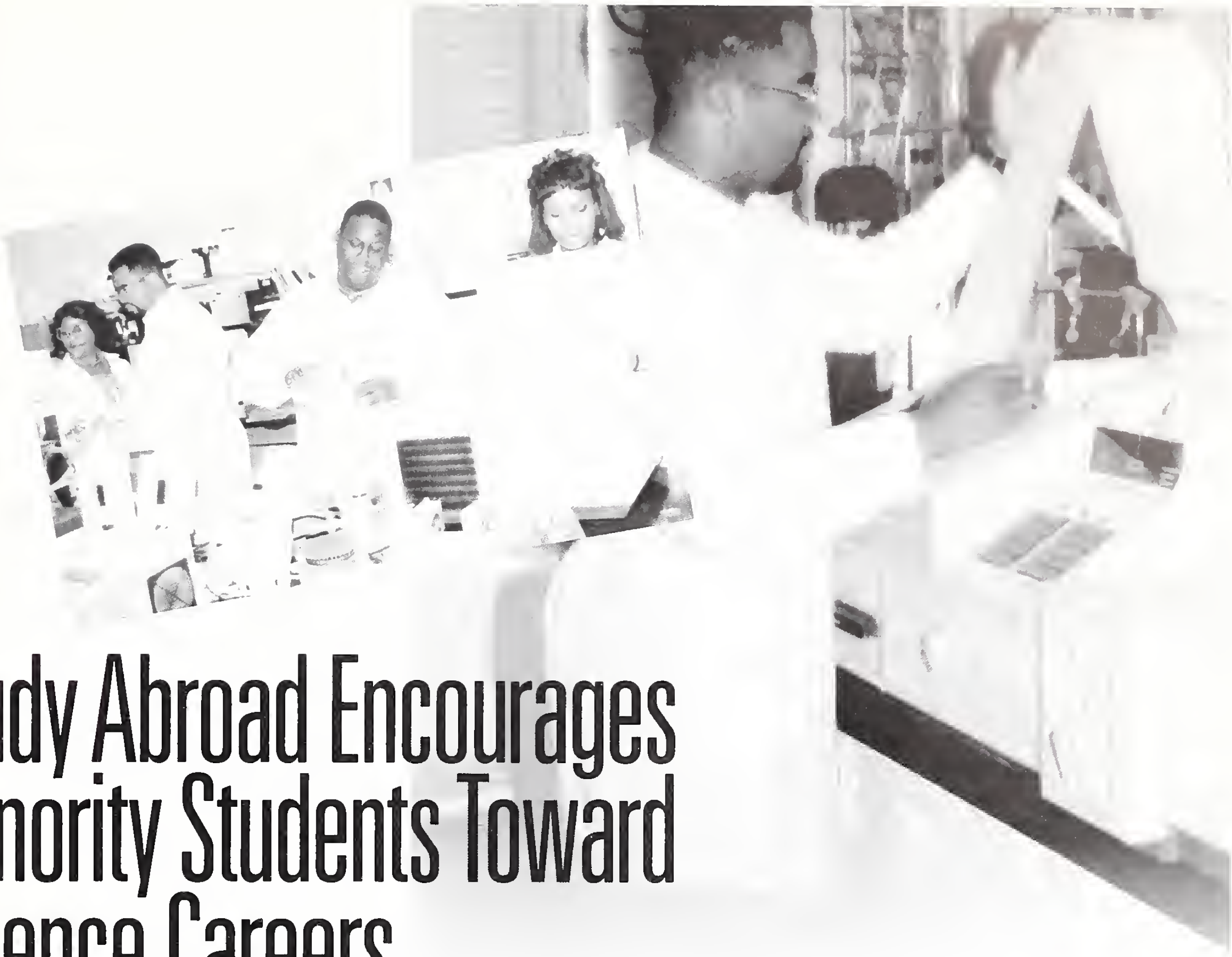
Institute scientist volunteers visit the schools to teach and train the students; during visits to NINDS, the students and teachers are exposed to some of the finest and most advanced biomedical research in the world.

The program enables students to acquire basic scientific skills and learn how those skills can be applied to real problems. A small number are invited to return to work in NINDS laboratories with institute scientists as participants in the NINDS's summer program.

The program's overall goals are to promote the study of science among high school students, and to encourage minorities to pursue research careers in the neurological sciences.

"The NINDS is committed to equal opportunity," said Levon O. Parker, Minority and Special Concerns Program Officer for the NINDS. "We feel it is important to establish a biomedical research environment that reflects the diversity in the American population. And so we have developed this and other programs to help create a cadre of minority and women neurological scientists for the next century."

Shannon Garnett, writer/editor, the National Institute of Neurological Disorders and Stroke.



Study Abroad Encourages Minority Students Toward Science Careers

> THE MIRT PROGRAM CONSISTS OF GRANTS THAT ARE AWARDED TO COLLEGES AND UNIVERSITIES THAT INDEPENDENTLY SELECT UNDERGRADUATE AND GRADUATE STUDENTS AND FACULTY MEMBERS TO CONDUCT SCIENTIFIC RESEARCH AT FOREIGN UNIVERSITIES OR RESEARCH CENTERS.

International study programs are known to be useful to students. They gain valuable experience and often learn techniques that may not be taught at their universities. However, as Dr. John Ruffin, NIH Associate Director for Minority Health Programs points out, "While international opportunities are becoming commonplace for students throughout the U.S., minority students are less likely to participate in study abroad programs than their non-minority counterparts."

The National Institutes of Health (NIH) is changing this.

In October 1992, the Fogarty International Center (FIC) and the Office of Research on Minority Health (ORMH) sponsored a workshop to consider the unique role international programs play in the recruitment, education, and training of minority students. As a result of workshop discussions, the Minority International Research Training Grants (MIRT) program was created.

The MIRT program consists of grants that are awarded to colleges and universities that independently select undergraduate and graduate students and faculty members to conduct scientific research at foreign universities or research centers. Explains Dr. Philip E. Schambra, FIC Director, "We created this program to encourage minority college students to choose careers in science, and we feel that by going abroad, many students will experience the excitement of scientific research in a global atmosphere."

Just over two years after the workshop, 26 training grants, totalling approximately $5.6 million, have been awarded, which include 46 colleges and universities in 22 states, the District of Columbia, and Puerto Rico. The three-year grants will enable approximately 250 students and faculty to collaborate with foreign research centers in 46 nations. NIH provides stipends, health insurance, foreign tuition and fees, and living and travel expenses under the awards.

Each award is unique and may include any or all of the following three components. First, the program is designed for undergraduate minority students pursuing life science curricula. Accompanied by faculty, these students will conduct research abroad for 8 to 12 weeks. Second, minority graduate students will receive predoctoral research training for 3 to 12 months at foreign institutions. Third, individual minority faculty will conduct research at foreign institutions for 3 to 12 months.

In a typical scenario, a group of six to eight undergraduate students from the same university travel to a foreign site accompanied by at least one faculty member. They conduct research in a laboratory and spend time together each week learning the country's language and customs. This time together gives students an opportunity to practice speaking and writing a foreign language and serves as a means of encouragement and support.

Wilveria B. Atkinson, Ph.D., Chair of the Department of Life Sciences at Winston-Salem State University in North Carolina, is the university's project officer for the MIRT grant. The award also covers three other institutions: Barber Scotia College, Bennett College, and Livingston College, all in North Carolina. Although the students have not yet been selected, Dr. Atkinson has experience with a similar program that sends minority students abroad to conduct basic science research. Dr. Atkinson believes that "a student's experience of conducting research abroad increases awareness of one's potential."

Students in the MIRT program conduct research in a laboratory and spend time together learning the country's language and customs.

The selection process for students and faculty to participate in the MIRT program is designed by the grantee university or college. At Winston-Salem State University the students must meet strict eligibility guidelines. According to Dr. Atkinson, students must have successfully completed two years of chemistry, one biochemistry course, and at least an introductory course in molecular biology. Additionally, students must have spent at least one summer working in research in the United States. Faculty eligibility may fall into one of two categories. They must either be currently involved in biomedical research and want to expand their area of competency, for example, by learning a new technique or, as a junior faculty member, they must want to establish a basic research program at the university.

In May 1993, three students from Winston-Salem State University spent two and a half months working with researchers at the Biotechnology Centre of Oslo at the University of Oslo in Norway. The students were given this opportunity through Project Strengthen, which was creatively funded by Winston-Salem State University. The school used profits from vending machines campus-wide to cover the costs of the program.

Micheala Jones, Travis Perry, and Carlos Privette praised their experience in international research, saying that it played an important role in confirming their interest in a science career. In fact, Travis' mentor in Norway, Dr. Ann-Britt Kolsto, convinced him to enter a M.D./Ph.D. program because it is useful for scientists to approach their research from both clinical and basic science points of view. Michaela and Carlos are also considering combined degrees.

Travis Perry speaks highly of his experience in Norway. In Dr. Kolsto's laboratory, Travis, then a college junior, learned a variety of research techniques and worked with graduate students sequencing and mapping the genome of a common bacteria. "Working and learning techniques in the laboratory helped me realize that research is an exciting career choice for me," commented Travis.

Track records of similar international study programs suggest that the MIRT program will do what it has set out to accomplish— to give minority students the opportunity to excel in the science and health professions. Concludes Dr. David Wolff, chief of the International Research and Awards Branch at the Fogarty International Center, "The university faculty and administrators see this program as an opportunity to attract undergraduate and graduate students into careers in biomedical research, preparing students for the 21st century by providing a truly global research training experience. On returning to their U.S. training programs, their work and careers in biomedical research will have added meaning."

Suzanne Lewis, public affairs specialist, the National Institute on Aging's Gerontology Research Center in Baltimore, MD.

ADDITIONAL RESEARCH SUPPORT

FROM THE
OFFICE OF RESEARCH ON MINORITY HEALTH
(ORMH)

Minority Health at NIH: Building Partnerships for the Future

D.C. Minority Infant Health Initiative

By the end of FY 1993, ORMH funded six centers under the Cooperative Community-Based Perinatal Studies and Interventions in Minority Program. Protocols for three major studies have been developed and are currently being initiated. The main focus of this research is to develop and test interventions to reduce infant mortality.

Health Behaviors of Minority Adolescents Initiative

The Minority Youth Health Behavior Research: The Development and Evaluation of Interventions Program is jointly conducted with the National Institute of Child Health and Human Development, and includes 7 research projects and one data center.

Minority Aging Centers

In FY 1993, the ORMH with the National Institute on Aging provided funding for 6 Exploratory Centers for Research on Health Promotion and Disease Prevention. Four of the six centers, which will focus on research to improve the health of older minorities, are funded by ORMH.

Minorities Benefit from Diabetes Research— ORMH is supporting research on the pathogenesis of NIDDM in Mexican American women and several community-based and primary prevention projects targeting Native Americans. The ORMH is also providing support for the Gestational Diabetes Component of the NIDDM Primary Prevention Trial and the New Mexico Clinical Center. In FY 1994, the ORMH provided funding to start-up a number of diabetes gene research grants to uncover the basis of diabetes in minority populations. In FY 1995, ORMH will contribute to the NIDDK effort to develop interventions for the treatment and prevention of diabetes in minorities.

Shortage of African American Oncologists Reflects Larger Problem—ORMH and the Office of the Director, NIH are supporting the Clinical Research Loan Repayment Program, which provides funds to pay off the educational loans of qualified minorities. In FY 1993, the ORMH supported the NCI Teacher Enrichment Program, designed to enhance the Adopt-A-School Partnership.

Centers Program Strengthens Research Capability of Minority Institutions—ORMH has provided support for the RCMI program to expand research in environmental sciences at Ponce School of Medicine, Puerto Rico; Clark Atlanta University, Georgia; and Meharry Medical College, Tennessee.

Research Provides Benefits to Minorities with Lupus—ORMH has provided support to a number of research projects on lupus. They include: Genetic Association with Lupus in American Blacks; Outcome of SLE in Minorities; Using Idiotypes to Assess SLE Activities in Minority Women, and others.

Researchers Write Primer on Challenges of Minority Recruitment—ORMH provided support to study factors influencing the participation of minorities in HIV vaccine trials.

Long-Running Programs Increase Number of Minority Scientists—In FYs 1993 and 1994, ORMH provided support to the MARC and MBRS programs.

Research and Education Combine to Prevent and Cure Asthma Among African Americans—In FYs 1993 and 1994, ORMH supported research on asthma prevention and intervention in African American, Hispanic, and Asian American groups.

Research Centers Established to Improve Minority Oral Health—ORMH has provided support for a meeting of the Directors of the Regional Research Centers for Minority Oral Health.

Student Programs Encourage Future Minority Scientists to Study Neurosciences—ORMH supports a Neurological Sciences Center at Morehouse School of Medicine in Atlanta for the study of locomotor control and associated disorders. The goal is to establish a major neuroscience training center for underrepresented minorities.

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Women and Drug Abuse: A National Health Priority

BY THE NIDA PRESS OFFICE

Drug abuse among women is a serious, continuing illness. However, women can recover from this disorder when treatment adequately meets their special needs, according to experts.

To further explore this issue, NIH's National Institute on Drug Abuse (NIDA) recently hosted a conference on "Drug Addiction Research and the Health of Women" to focus attention on the unique impact of drug use, abuse, and addiction on women's health.

Speaking at the conference, NIDA Director Dr. Alan Leshner said, "Drug addiction is a chronic, relapsing problem which may progress differently in women of all ages, not just those of childbearing age."

Evidence of health risks from drug abuse throughout a woman's lifespan were cited. Women who use drugs are often underweight or malnourished, depressed, have been physically abused by their partner, and are at risk for sexually transmitted diseases and HIV/AIDS.

Pregnant drug abusers are also at increased risk for ectopic (tubal) pregnancy, stillbirth, low weight gain during pregnancy, miscarriage, hypertension, anemia and other medical problems. Their newborns may have lower birth weight and smaller head size than babies born to healthy mothers.

A major factor in keeping women drug abusers from seeking or accepting treatment is their role as caretakers of children, elderly parents, or other relatives. Women also may not seek treatment out of fear of prosecution by the legal system, and fear they will lose their children, concerns that are well-founded, according to the conference presenters.

Even when women do seek treatment, they face long waiting lists and find that many programs will not accept pregnant women. Further, poor women often have no health insurance and no way of paying for treatment.

When drug-abusing women *can* find and *do* accept treatment, they benefit most from programs that address not only their chemical dependency, but provide services that meet their basic needs, such as food, clothing, shelter, child care, and medical care. An individually-tailored, pharmacological/behavioral approach, linking health care and HIV services as well as drug treament, stands the best chance of success, said conference experts.

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According to Dr. Loretta Finnegan, Director of NIH's Women's Health Initiative, "Almost half of all women who have ever used illicit drugs are in the childbearing age of 15 to 44. Therefore, it is important to understand the epidemiological issues of these women, including their drug use during pregnancy."

Consequently, as part of the conference, NIDA released findings from its "National Pregnancy and Health Survey," the first comprehensive analysis of drug use among pregnant women. Key findings include:

- In 1992, 221,000 women who gave birth (5.5 percent) used an illicit drug during pregnancy;
- The two most frequently used drugs were marijuana, 119,000 women (2.9 percent) and cocaine, 45,000 women (1.1 percent);
- About 757,000 (18.8 percent) of the women drank alcohol and 820,000 (20.4 percent) smoked cigarettes at some time during pregnancy. These results demonstrate a strong link between the use of illicit drugs and alcohol and tobacco use.

Survey results also pointed to issues of prevalence differences among ethnic minorities. The estimated number of white women using drugs during pregnancy was much higher than the number of African American or Hispanic women. Rates of cocaine use (in particular, crack—cocaine pellets that are smoked) however, were considerably higher among African American women than for white or Hispanic women.

The survey also found that despite a generally decreasing trend in drug use from 3 months before and throughout the pregnancy, there was no total discontinuation of drug use. "This is an indicator of how gripping an illness drug addiction can be, even in the face of what may seem to be the ultimate incentive to stay drug-free," noted Leshner.

"Drug addiction has a strong effect on a user, both biologically and behaviorally, but it is a disease that can be treated and managed," Leshner concluded. Findings from other NIDA research indicate that once successfully detoxified and enrolled in a treatment program, the focus of the lives of drug-abusing women changes dramatically from their drug use to their children. ▲

A summary of conference presentations will be available in late 1995 from the National Clearinghouse on Alcohol and Drug Information (NCADI), 1-800-729-6686. NIDA's National Pregnancy and Health Survey will be available from NCADI later this summer.

NIH RESEARCH CAPSULES

Small Reductions in Blood Pressure Could Save Lives

Just a slight decrease in diastolic blood pressure could help thwart coronary heart disease and stroke nationwide, say researchers supported by NIH's National Heart, Lung, and Blood Institute (NHLBI).

High blood pressure is a major risk factor for both heart disease and stroke, the first and third leading killers of Americans. It also contributes significantly to kidney failure. Declines over the past several decades for both heart disease and stroke can be attributed, in no small measure, to increased awareness and better control of high blood pressure.

Currently, more than half of all cardiovascular events occur in persons with normal blood pressure levels. Prevention efforts aimed at those with lower levels could result in further declines.

Investigators, led by Dr. Nancy R. Cook of the Brigham and Women's Hospital in Boston, MA, used existing data from the Framingham Heart Study and the National Health and Nutrition Examination Survey II (NHANES II) to estimate the overall impact of small reductions in diastolic blood pressure on the incidence of stroke and heart disease.

The researchers calculated that a nationwide, 2-mm Hg reduction in diastolic blood pressure would result in 17 percent fewer cases of hypertension. For white men and women 35 to 64, this 2-mm Hg decline by itself could ward off almost as many strokes and cardiac events as conventional medical treatment. Further, combining the 2-mm Hg population drop with medical intervention could double or even triple the impact of medical therapy alone, the investigators say.

In conclusion, the scientists believe that everyone with diastolic pressures above 70-mm Hg could benefit from lowering these values by about 2-mm Hg. In many cases this could be accomplished by low-risk interventions such as moderate weight loss and exercise. As a result, about 67,000 cases of heart disease and 34,000 cases of stroke could be prevented each year in middle-aged Americans, the researchers say.

For recorded information on the prevention and treatment of high blood pressure, call NHLBI's National High Blood Pressure Education Program on 1-800-575-WELL.

Ref: Cook, N.R., ScD., et al., "Implications of Small Reductions in Diastolic Blood Pressure for Primary Prevention," ***Archives of Internal Medicine****, Vol. 155, pp. 701-709, April 10, 1995.*

Miscarriage Risk Rises With Unprotected Nitrous Oxide Exposure

Regular occupational exposure to nitrous oxide puts pregnant dental assistants at more than double the risk for a spontaneous abortion. However, proper ventilation may alleviate this health threat, according to a study conducted by NIH's National Institute of Environmental Health Sciences (NIEHS).

Nitrous oxide has long been suspected of having potentially toxic effects on the reproductive system, although previous studies have shown inconsistent results. The medication, employed primarily to relieve anxiety in dental patients, is used in about half of all dental offices.

This study, conducted by Drs. Andrew S. Rowland, Donna D. Baird and their colleagues in Research Triangle Park, NC, looked at the association between nitrous oxide exposure and spontaneous abortion among 1,465 dental assistants aged 18-39 who became pregnant while working full time.

One hundred and one of these women reported having a miscarriage during the period. The risk of miscarriage was increased by more than 2½ times for women who worked with nitrous oxide in offices without scavenging (venting) equipment. There was no such increased risk among those working in offices where this equipment was in place. An earlier analysis of data collected from this same group of dental assistants found that nitrous oxide impaired fertility among women using the gas without venting equipment.

The scientists conclude that venting equipment appears to be important in protecting the reproductive health of women who work with nitrous oxide.

*Ref: Rowland, A.S., et al., "Nitrous Oxide and Spontaneous Abortion in Female Dental Assistants," **American Journal of Epidemiology**, Vol. 141, No. 6, pp. 531-537, 1995.*

Tight Glucose Control Helps Prevent Diabetes-Related Nerve Damage

Insulin-dependent diabetic individuals who undergo strict, intensive treatment of their condition markedly reduce their risk for diabetic neuropathy. Such nerve damage can give rise to infection, foot and leg ulcers, and in advanced cases, limb amputation. This finding is taken from the Diabetes Control and Complications Trial (DCCT), an investigation supported by NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

The DCCT involved 1,441 people, ages 13 to 39, who had insulin-dependent diabetes. Seven hundred twenty-six of them had diabetes for 1 to 5 years and entered the study with no concurrent retinopathy or other retinal disease (primary prevention group); 715 had diabetes for 1 to 15 years and developed mild to moderate retinopathy (secondary intervention group).

Diabetic retinopathy is a disease of the retina, the light-sensing tissue at the back of the eye. The disorder can damage the tiny vessels that normally furnish the retina with blood, causing blurred vision, detachment of the retina, or vision loss. Early detection and treatment of diabetic retinopathy is vital.

For the purpose of the trial, participants were randomly divided into two diabetes management plans: an intensive therapy group that took at least three daily insulin injections (or used an external insulin pump) and tested their blood glucose at least four times a day. They also made monthly visits to their doctor. The objective was to keep blood glucose levels as close to normal as possible. Participants in the conventional therapy group took one or two daily injections of insulin, checked glucose levels or urine less frequently, and saw their physician four times a year. Their goal was to maintain clinical stability–that is, no symptoms of high or low blood sugar while preserving normal development.

At the time of follow-up five years later, the investigators, using nerve conduction tests, clinical examination, history, and autonomic nervous system tests found that 13 percent of the subjects in the conventional therapy group had developed diabetic neuropathy. Meanwhile, only five percent in the intensive therapy group had done so. Thus, intensive therapy lessened the likelihood for developing this debilitating condition by 64 percent.

Results reported earlier from the DCCT demonstrated that tight glucose control, or intensive therapy, also slows the rate of progression and lowers the incidence of diabetes-related eye and kidney complications in both adults and children. The treatment may, however, cause low blood sugar, or hypoglycemia–an acute condition that usually responds to rapid ingestion of a sugar-rich substance.

Ref: "The Effect of Intensive Diabetes Therapy on the Development and Progression of Neuropathy," the Diabetes Control and Complications Trial Research Group, ***Annals of Internal Medicine****, Vol. 122, No. 8, pp. 561-568, April 15, 1995.*

Schizophrenia Drug Continues to Benefit Some

Findings from two recent studies supported by NIH's National Institute of Mental Health (NIMH) confirm that the antipsychotic drug clozapine (Clozaril, TM) provides symptomatic relief for many patients who fail to improve sufficiently or cannot tolerate the standard medications prescribed for schizophrenia.

About two million Americans suffer from this disorder. Symptoms may include anxiety and confusion, delusions, hearing voices or other hallucinations, disordered patterns of thinking, inappropriate behavior or apathy ("flat affect"), and social isolation. Patients often have difficulty separating reality from their hallucinations and/or delusions, and may experience multiple cycles of remission and relapse.

While treatment normally begins with trials of standard antipsychotic medications such as haloperidol (Haldol, TM), these drugs often have troubling side effects such as tardive dyskinesia (abnormal movements, especially of the mouth or tongue), or they may simply be ineffective.

Clozapine was approved for treating schizophrenia in 1993, and has since shown great promise for some patients. One principal advantage of the drug is that it usually does not cause tardive dyskinesia or other adverse reactions as do the standard antipsychotic medications. However, a dangerous side effect, though rare, is agranulocytosis, a potentially fatal white blood cell disorder that may strike about one percent of clozapine users. Patients receiving clozapine must undergo weekly blood tests to monitor this reaction.

Dr. Jeffrey A. Lieberman and his colleagues at the Long Island Jewish Medical Center in Glen Oaks, NY, recently conducted a year-long investigation of 84 schizophrenic patients who were administered clozapine. Sixty-six patients had treatment-resistant schizophrenia, while 18 experienced side effects from other medicines. The researchers found that the medication significantly reduced delusions, hallucinations, and related symptoms in 50 percent of the former and 76 percent of the latter group.

The rate and type of side effects varied among patients but many reactions resolved over time. The most serious side effects included seizures (6 subjects) and agranulocytosis (7 subjects). Overall, treatment responses were poorer among patients who fell ill at a relatively young age, and for females.

In another protocol, Dr. Robert G. Stern and his associates at the Bronx VA Medical Center and Mount Sinai School of Medicine in New York found that an early, positive response to clozapine often predicted longer-term success.

For five weeks the researchers administered the drug to 40 treatment-resistant schizophrenia patients (33 men and 7 women), assessing drug efficacy after both one week and five weeks. They found that of those patients demonstrating a favorable response after one week, 75 percent showed sustained benefits after the fifth week. Further, those afflicted with the most severe symptoms at the start of the study, and patients exhibiting the greatest improvements following week one were most likely to show resolution of symptoms after week five.

The high predictive rate of treatment response after week one is significant for treatment. When agranulocytosis develops, for example, symptoms usually do not appear until after the fourth week of clozapine therapy. If clozapine treatment response *can* be accurately predicted after the first week, those not responding could be withdrawn from the drug before developing the often fatal blood cell disorder.

Refs: Lieberman, J., M.D., et al., "Clinical Effects of Clozapine in Chronic Schizophrenia: Treatment Response and Predictors of Outcome," ***American Journal of Psychiatry****, Vol. 151, No. 12, pp. 1744-1752, Dec. 1994.*

Stern, R.G., M.D., et al., "Early Response to Clozapine in Schizophrenia," ***American Journal of Psychiatry****, Vol. 151, No. 12, pp. 1817-1818, Dec. 1994.*

Exercise Lowers Risk for Diabetes, Major Study Indicates

Participating in physical activity on a regular basis sharply curbs the risk for developing diabetes, suggest results of a comprehensive, longitudinal study of nearly 7,000 middle-aged men. The research was conducted by scientists with NIH's National Heart, Lung, and

Blood Institute in Honolulu, HI.

While exercise has been shown to improve cardiac, lung, and muscular performance, few long-term studies have assessed its effects on the development of non-insulin dependent diabetes. However, short-term investigations have suggested that exercise wards off the disorder.

A team of researchers led by Dr. Cecil M. Burchfiel examined the link between physical activity and diabetes in 6,815 middle-aged Japanese-American men participating in the Honolulu Heart Program. All were initially free of clinically diagnosed diabetes in 1965-68. The subjects' activity levels and overall health status were then tracked for the next six-and-a-half years.

After adjusting for possible confounding factors, such as family history of diabetes, age, obesity, systolic blood pressure, and glucose levels, the investigators found that exercise significantly decreased the incidence of diabetes. When comparing subjects who exercised most with those who exercised least, those in the former group had only about half the risk for developing diabetes compared to the less active individuals. This result held for older men (55–68 years of age), as well as for younger ones (45–54 years).

Evidence indicates that exercise or aerobic conditioning increases the body's overall sensitivity to its own insulin, a key protein produced by the pancreas, thus decreasing insulin resistance. Insulin resistance occurs when an individual must produce more insulin than normal to move glucose into the muscle cells. When the body cannot manufacture enough insulin (often due to significant weight gain), blood sugar levels rise and diabetes develops.

Regular physical activity also helps to moderate body weight. Sixty to ninety percent of individuals with adult-onset diabetes are overweight.

Ref: Burchfiel, C.M., Ph.D., et al., "Physical Activity and Incidence of Diabetes: The Honolulu Heart Program," **American Journal of Epidemiology**, *Vol. 141, No. 4, pp. 360-368, 1995.*

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Vulvodynia, A Little Known But Perhaps Widespread Cause of Distress in Women

BY JAN EHRMAN

Although the condition has probably occurred for at least a century, vulvodynia was not defined in medical circles until 1983. Only recently have women begun seeking treatment for the disorder, characterized by a sensation of severe burning, pain, or stinging of the vulva—the female external genital organs, (the labia majora, labia minora, and clitoris).

While rates are unknown, the incidence of vulvodynia (different from "pruritis vulvae" or chronic vulvar itching) is thought to be high. "In one private practice, 15 percent of patients making first time visits complained of vulvar discomfort," according to Dr. Maria Turner of the National Cancer Institute. She discussed the condition at a recent lecture at the National Institutes of Health.

The disorder is not limited to women in the United States. Turner reported cases in South Africa, England, and Australia.

Vulvodynia has remained somewhat a medical enigma, in part because its cause is often not known. Until recently, many doctors, unable to make a diagnosis or provide symptomatic relief, often referred patients complaining of vulvar discomfort for psychiatric help. While vulvodynia may have psychological components, experts now agree that the symptoms are primarily physical. In addition, the disorder often plays havoc with the woman's quality of life, and can be especially detrimental to marital and sexual relations.

In some cases, women with vulvodynia may develop lesions or open sores on the skin surrounding the vulva. Women receiving cancer chemotherapy and those with lupus (an autoimmune disorder that predominantly strikes women) may experience these symptoms. "These cases are usually clear-cut and not diagnostic problems," said Turner.

Other women may have a more troubling form of the disease known as vulvar vestibulitis. The condition appears as erythema (redness, irritation), with small, red patches in the vulvar region. Among women, usually in their twenties or thirties, these abrasions and related pain may arise from intercourse, from wearing tight-fitting pants, using tampons, or bike riding. Causes may also include a recurrent yeast infection, trauma, such as from caustic chemicals, or laser surgery for

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vulvar genital warts or similar conditions. Most often, however, the etiology remains unknown.

Symptoms may disappear on their own within 6-12 months. Meanwhile, a conservative treatment approach is preferred, said Turner. Since overcleansing may be a factor, she believes that patients should discontinue using any soaps, douches, sprays, or medications. A topical anesthetic may be useful prior to intercourse.

For chronic cases of vulvar vestibulitis, injections of alpha-interferon into the lesions may be beneficial. Studies indicate it reduces or eliminates symptoms in about one-third of patients. The alternative therapy for unremitting problems is surgery—modified perineoplasty (removal of the vulvar vestibule, the inner part of the vulva), which has a 60–85 percent success rate.

In another form of the disease (pudendal neuralgia), burning or stabbing pains, or tingling/numbness may develop in the vulvar region. This is thought to be a form of nerve pain. The cause is generally unknown, although occasionally recurrent genital herpes, or trauma, either surgical (e.g., episiotomy) or accidental may be to blame. This condition may be more difficult to diagnose "since there are usually no observable physical signs," said Turner. "Meanwhile, even mild genital contact, such as gentle wiping with tissue paper or a cotton ball can cause extreme discomfort," she added.

Treatments include the use of tricyclic antidepressants, and, less often, anticonvulsant drugs. Those with recurrent genital herpes may be helped by the anti-viral agent acyclovir. These medications have shown success when used by themselves or in combination.

While treatments are available, finding a physician who is knowledgable about vulvodynia may pose a challenge. Turner recommends that women with persistent vulvar discomfort should first report it to their physician. If he or she cannot help, an alternative is to check with the departments of gynecology or dermatology at a nearby medical school to see if they have clinicians who specialize in treating disorders of the vulva. ▲

Jan Ehrman is editor of ***NIH News and Features****.*

Editor's Note: *Dr. Maria Turner and her colleagues are conducting a study at the NIH Clinical Center in Bethesda, MD, and are currently seeking female subjects who suspect they have vulvodynia. Women from Maryland, Virginia, and Washington, DC interested in participating are encouraged to contact Dr. Turner on (301) 496-6421.*

The Mysteries of Sepsis: Seeking to Understand the Process of Blood Poisoning

BY RUTH LEVY GUYER

It will probably take multiple therapies to adequately combat sepsis, the blood poisoning that takes the lives of 100,000 Americans annually, says Dr. Richard Ulevitch, of the Scripps Research Institute in La Jolla, CA. Ulevitch is a grantee of the National Institute of General Medical Sciences (NIGMS).

Sepsis is brought on by one of the most potent bacterial toxins known, LPS (lipopolysaccharide), a chemical that is released into the blood by many different bacteria. Even with aggressive therapies, including antibiotics and intravenous fluids, the effects of LPS are often overwhelming.

In injured, sick, and burned patients, LPS packs the powerful punch that can lead to sepsis. A chain reaction begins—the body's cells release LPS, tissues become inflamed, and organs decay. Fifty percent of all sepsis patients die when efforts by the immune system to react to the bacterial infection and release of LPS fail.

> *"I am optimistic that therapies that disrupt the interactions of LPS-LBP complexes with DC14 could be helpful in the treatment of sepsis," says Ulevitch.*

Scientists have known about LPS for a century (it was formerly called endotoxin), but only recently have they begun to understand how it triggers sepsis. They are not sure exactly what it will take to derail the disorder, however Ulevitch proposes that it may require a combination of therapies. He and his co-workers have spent the last 15 years looking for new targets for such therapeutic intervention.

One of the more intriguing routes to sepsis the group has recently found involves immune system (infection-fighting) cells called macrophages and monocytes (M cells). LPS can activate these cells directly. But if LPS first links up with a protein in the blood called LBP, immune cells activate at significantly lower LPS levels, and sepsis is triggered faster.

Ulevitch has found that after LBP and LPS combine, they locate and bind to a receptor called CD14 anchored in the outer membrane of an M cell. This interaction, in turn, sends signals through the membrane and through the cell to the nucleus (a process called "signal transduction"), where genes are turned on and new proteins are produced. Some of the proteins, called mediators, are released by the cell and fan out to other cells, which they activate. This chain reaction generates the raging fevers, dangerously low blood pressure, organ failure, and other characteristics of sepsis.

"I am optimistic that therapies that disrupt the interactions of LPS-LBP complexes with CD14 could be helpful in the treatment of sepsis," says Ulevitch. He suggests that it might be possible to "mop up" LPS or its complexes in the blood

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with blocking agents, thereby keeping the complexes from binding to and activating cells.

If sepsis cannot be "nipped in the bud," adds the scientist, opportunities may exist to halt signal transduction or the more advanced stages of the condition.

Although disarming sepsis will not be easy, researchers like Ulevitch and others are hopeful they are moving closer to new and effective therapies. ▲

For more information on sepsis, contact: Information Office, National Heart, Lung, and Blood Institute, NIH, 9000 Rockville Pike, Building 31, Room 4A-21, Bethesda, MD, 20892, phone: (301) 496-4236.

Ruth Levy Guyer is a writer in the biological sciences with NIH's National Institute of General Medical Sciences.

NIH RESEARCH CAPSULES

Vitamin A Supplements Help RP Patients Preserve Sight Longer

Taking moderate, supplemental amounts of vitamin A (palmitate) enables patients with retinitis pigmentosa (RP) to slow the progression of the disease, according to a clinical trial conducted by National Eye Institute grantees.

RP is a hereditary disorder of the retina that leads to night blindness in adolescence, and ultimately, greater loss of vision or total blindness later in life. The condition affects approximately 100,000 Americans and nearly 1.5 million people worldwide. Currently there is no cure, although vitamins or other dietary therapy may be beneficial, some authorities have suggested.

In a randomized, double-masked study involving 4 treatment groups totaling 601 RP patients, Dr. Eliot L. Berson and his associates from the Department of Ophthalmology at the Harvard Medical School found that adults (aged 18-49) who ingested 15,000 international units (IU) of vitamin A daily experienced a 20 percent slower annual decline in retinal function than participants not taking the supplement. The study lasted 6 years.

Based on that finding, the researchers estimate that a patient who began taking 15,000 units of vitamin A daily at age 32 would retain some useful vision until age 70. In contrast, an RP patient not taking this dose would lose vision at age 63.

The scientists caution, however, that consuming more than 15,000 units daily of vitamin A does not provide added benefits, and could actually be harmful. Further, they advise against taking vitamin A supplements during pregnancy, due to their reported link to birth defects.

*Ref: Berson, E.L., M.D., et al., "A Randomized Trial of Vitamin A and Vitamin E Supplementation for Retinitis Pigmentosa," **Archives of Ophthalmology**, Vol. 111, pp. 761-772, June 1993.*

Depression May Co-Exist With Asymptomatic Hypothyroidism

Individuals with untreated subclinical hypothyroidism—an underactive thyroid gland not so deficient as to meet the clinical criteria for the overt form of the disease—may be vulnerable to depression, say researchers supported by the National Institute of Mental Health.

Hypothyroidism is a somewhat common, potentially serious disorder that causes lethargy, weight gain, and symptoms with even greater health consequences, such as depression. A subset of this disease is the more common subclinical hypothyroidism, in which the thyroid is somewhat underactive, but without symptoms. At least 1 out of 20 persons have subclinical hypothyroidism.

Since depression is associated with overt hypothyroidism, can the mental disorder also be brought on by or co-exist with the subclinical form?

Dr. John J. Haggerty, Jr. and his colleagues from the University of North Carolina School of Medicine in Chapel Hill, analyzed the lifetime history of depression in 31 women—16 otherwise

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healthy adults diagnosed with (untreated) subclinical hypothyroidism, and 15 healthy (control) subjects with no thyroid abnormality.

Their data revealed that subjects diagnosed with subclinical hypothyroidism were nearly 3 times as likely to have experienced a depressive episode at some time during their life, compared to controls (56 percent vs. 20 percent).

The researchers theorize that subclinical hypothyroidism, while not always a direct cause of depression, may lower the threshold for the mental disorder. Future studies will help determine if thyroid replacement therapy is appropriate for these comorbid patients.

Ref: Haggerty, J.J., M.D., et al., "Subclinical Hypothyroidism: A Modifiable Risk Factor for Depression?", ***American Journal of Psychiatry****, Vol. 150, No. 3, pp. 508-510, March 1993.*

Older Age, Anxiety, Less Education, Inhibit Mammography in Some High-Risk Women

While most younger women at high (genetic) risk for breast cancer receive regular mammograms, older high-risk women and those with less schooling frequently do not. In a study supported by the National Cancer Institute, more than 1 out of 10 had *never* received this critical diagnostic exam.

Experts say that about 1 out of 5 breast cancers have a genetic or familial component. They also maintain that while all women are at risk of developing breast cancer, those who have a first-degree relative with the disease have a risk that is increased 2 to 10 times. Mammography, or breast x-rays, however, can often detect very small, incipient breast cancers. Such early detection with treatment greatly improves the outlook for less radical surgery and increases the chances for recovery.

A research team, led by Dr. Caryn Lerman from the Fox Chase Cancer Center in Philadelphia, PA, investigated mammography practices in 140 women, 35–79 years of age, each of whom had a first-degree relative with breast cancer. They matched frequency of screening with age, and such psychological variables as depression, anxiety, and overall breast cancer concerns. Educational level was also attained for comparison purposes.

The researchers found that younger subjects were generally prudent about mammograms. More than three-fourths of women in their mid-to-late thirties adhered to the prescribed mammogram schedule; 82 percent of them had received a mammogram within the past year.

However, more than one-third (37 percent) of older high-risk women (50 years and over) did not obtain regular mammograms. Those with serious breast cancer concerns or anxiety, and those with a high school education or less were also much less likely to obtain regular mammograms.

The results of this study, the first of their kind, point to an inverse link between psychological distress and mammography screening practices, indicating that breast cancer anxiety may hinder use of mammography. Follow-up investigations may help target appropriate psychoeducational interventions for such high-risk women, explain the scientists.

Ref: Lerman, C., Ph.D., et al., "Mammography Adherence and Psychological Distress Among Women at Risk for Breast Cancer," ***Journal of the National Cancer Institute****, Vol. 85, No. 13, pp. 1074-1080, July 7, 1993.*

Stress-Induced Breathing Changes and Hypertension

Episodes of slow, shallow (inhibitory) breathing in response to stressful events result in increased blood pressure in humans, according to researchers at the National Institute on Aging (NIA) in Baltimore.

Inhibitory breathing causes a rise in the blood concentration of carbon dioxide levels. Scientists believe that the increase in carbon dioxide, which makes the blood more acidic, may lead to increased sodium retention. This in turn may help explain the link between high salt consumption and increased blood pressure.

Dr. David E. Anderson and his colleagues at the NIA's Gerontology Research Center used portable monitoring equipment to measure the breathing frequency, activity, and tidal volume—the amount of air that fills the lungs with each breath—in human subjects with normal blood pressure. The monitors automatically recorded data during a 12-hour period.

At each blood pressure recording (every 30 minutes) participants updated their diaries providing information about posture, location, and social interactions. Subjects participated in a day representative of their typical schedule.

Participants at work or in a social situation showed more episodes of low-frequency breathing than when they were at home or alone. The study further demonstrated that low-frequency breathing during a normal day correlates with increased blood pressure, although not with increased heart rate, as seen in the "fight or flight" response.

Recent studies have also shown that this breathing pattern increases retention of sodium ions in the kidney (thus altering the body's water/sodium balance). This ultimately affects hormones which regulate the flow of sodium ions in the cells. The breathing pattern may also affect blood vessel constriction, in turn, increasing blood pressure.

The next step, according to the NIA research team, will be to determine if low-frequency breathing plays a direct role in sodium regulation and long-term control of blood pressure.

Ref: Anderson, D.E., Ph.D., et al., "Blood Pressure During Sustained Inhibitory Breathing in the Natural Environment," ***Psychophysiology****, Vol. 30, pp. 131-137, 1993.*

Higher Doses of Methadone Useful for Opioid Abusers

Opioid-dependent individuals may require moderate to high doses of methadone, 50 mg. or greater, to quell their drug habit, say scientists supported by the National Institute on Drug Abuse.

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NIH RESEARCH CAPSULES

More than half a million Americans regularly use opioids, such as heroin. Although methadone, an oral, synthetic opioid helps curb drug use and resultant behaviors (e.g., criminal activity), debate continues over what constitutes a therapeutic dosage. Some experts contend that currently prescribed dosages are often too low to be fully effective.

In a randomized, double-blind, placebo-controlled study, Dr. Eric C. Strain and associates from the Johns Hopkins University School of Medicine in Baltimore examined several different methadone dosages to determine their independent effect upon whether subjects remained in the drug-treatment program, and illicit drug use in 7 opioid-dependent patients with a h rate of cocaine use. Patients also eived counseling and group therapy.

Results of the 20-week program indicated that retention rates were higher in patients taking 50 mg. doses (52.4 percent), compared to subjects taking 20 mg. and placebo (41.5 and 21 percent, respectively).

Further, drug use rates, obtained through urine tests, showed that 50 mg. of methadone was significantly more effective (though not entirely successful) than the lower dose and the placebo in reducing the incidence of both opioid and cocaine use.

Acknowledging the dose-response effect of methadone for mixed opioid and cocaine abuse in the current study, the investigators suggest that additional research be conducted testing even larger amounts of methadone, which may ultimately be required to attain optimal therapeutic results.

*Ref: Strain, E.C., M.D., et al., "Dose-Response Effects of Methadone in the Treatment of Opioid Dependence," **Annals of Internal Medicine**, Vol. 119, No. 1, pp. 23-27, July 1, 1993.*

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Blood Transfusions May Raise Cancer Risk in Older Women

BY MARY SULLIVAN

Blood transfusions may increase the risk for certain types of cancer in older women, according to researchers supported in part by the National Cancer Institute (NCI).

Dr. James R. Cerhan and his colleagues at the University of Minnesota and the University of Iowa report from their study that the risk for non-Hodgkin's lymphoma and kidney cancer was greater in women ages 55–69 who had prior transfusions.

Research has shown that recipients of organ transplants, and other individuals whose immune systems are suppressed, are at increased risk for certain cancers. Moreover, some studies have indicated that patients who receive blood transfusions for cancer surgery have a higher risk of cancer recurrence. According to the researchers, this is the first investigation to specifically explore the relationship between transfusions and an increased risk for cancer.

The scientists obtained information from more than 37,000 women who participated in the 1986 Iowa Women's Health Study, part of a larger NCI-funded prospective study of breast cancer. The women were asked if they had ever received a blood transfusion, their age at first transfusion, and the reason for this procedure. Cancer cases were subsequently confirmed through the Iowa State Health Registry, in NCI's cancer registry program.

Their results showed that 25 percent of the women had a prior transfusion, at an average age of 37. The most common reason for the transfusion was blood loss from surgery, in many cases due to pregnancy complications.

The researchers report that during the five-year follow-up period (1986–1991), when a total of 1,816 cancer cases were reported, women with a history of transfusion were found to have approximately twice the risk for non-Hodgkin's lymphoma, and two and a half times the risk for kidney cancer, compared with women who had not received a transfusion. They also note that although a wide range of time periods occurred between the first transfusion and cancer diagnosis among the women, the greatest risk occurred within five years of the transfusion and decreased after that.

No increased risk was found for other types of cancer, including the most common in women—breast, lung, and colon.

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"The transfer of a carcinogenic (cancer-causing) agent, such as a virus or chemical contaminant, might account for the increase in risk," explains Cerhan. "Alternatively, changes in the immune system as a result of the transfusion may be responsible. We know that transfusions decrease the rate of organ rejection and increase susceptibility to infection."

Individuals with non-Hodgkin's lymphoma (a cancer of the immune system) are particularly susceptible to immune suppression. Although an explanation for the increased risk for kidney cancer is less clear, say the scientists, cases have previously been reported among transplant patients and other immune-suppressed individuals.

The researchers add that their results do not necessarily mean that blood transfusions pose a significant cancer risk for all patients who have received them. "The overall risk for non-Hodgkin's lymphoma is very low, with or without a history of transfusion, and kidney cancer is relatively rare," adds Cerhan.

Their future efforts will focus on non-Hodgkin's lymphoma to determine which type of transfusion—whole blood or blood component—poses the greatest risk, and whether the risk is affected by the number of units transfused or by the medical reason for receiving the transfusion. ▲

This research was published in the July 1, 1993 issue of **The Annals of Internal Medicine.**

For more information on cancer, contact: Information Office, National Cancer Institute, NIH, 9000 Rockville Pike, Building 31, Room 10A-18, Bethesda, MD, 20892; phone: (301) 496-5583. For information on blood transfusions, contact: Information Office, National Heart, Lung, and Blood Institute, NIH, 9000 Rockville Pike, Building 31, Room 4A-21, Bethesda, MD, 20892; phone: (301) 496-4236.

Mary Sullivan is a public affairs specialist with NIH's Office of Communications.

Homeless Women Found Resilient, Despite the Odds

BY BERNARDINE A. MOORE

In spite of the chronic and severe stress experienced by women who are homeless, the majority do not suffer from major mental illness. Their resilience speaks to the likelihood that important factors other than psychiatric disorders contribute to their homelessness, say researchers.

In one of the first studies to focus on psychiatric comorbidity (alcohol or drug abuse with a major mental disorder) in a population of homeless women, Dr. Elizabeth M. Smith and her colleagues at the Washington University School of Medicine, St. Louis, MO, reported that 51 percent of those interviewed had no lifetime *history* of substance abuse or a major psychiatric disorder. Further, 60 percent said they were free of any *current* major psychiatric problems, including alcohol or drug abuse.

The researchers also found that although the lifetime rate of psychiatric illness in the homeless women interviewed was nearly twice that of women in the general population, "their resilience is reflected in the rates of those untouched by psychiatric illness, even though these women have faced extraordinary stressors," says Smith. The study was supported in part by the National Institute on Alcohol Abuse and Alcoholism.

The higher lifetime rates of psychiatric illness found among the homeless women were due mostly to substance abuse and depression. "The low rates of other major mental disorders argue against previously published notions of severe mental illness and deinstitutionalization as major causal factors in homelessness," Smith asserts.

The higher lifetime rates of psychiatric illness found among the homeless women were due mostly to substance abuse and depression.

Despite some lower than expected rates of mental illness and substance use disorders, nearly one in three of the homeless women in the study had a history of substance abuse. In the area of comorbidity, the researchers found that of the homeless women with a psychiatric disorder, 44 percent also had a substance abuse disorder. In addition, nearly one-third of the women experienced posttraumatic stress disorder over their lifetime. According to the study, then, even though the lifetime and current prevalence rates of major mental illnesses or personality disorders is low overall, many homeless women do experience some serious problems.

Recent estimates show that women make up nearly 25 percent of homeless individuals in the United States. For this study, 300 homeless women from St. Louis shelters were randomly selected and interviewed. Rates of psychiatric diagnoses in these subjects were compared with rates in the general population of women in St. Louis.

The researchers found that multiple periods of homelessness—periods lasting until the woman had lived at least a month in her own home, apartment or

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room—were frequent. Almost one-fifth of the women had experienced more than four homeless episodes.

The women interviewed were predominantly Black, reflecting the ethnic composition of the inner city of St. Louis where the shelters are located and where most of the women lived before becoming homeless. The majority were young, single, and had at least one child under the age of 16 living with them. Most of the women supported three other people besides themselves on their income. More than three-fourths (77 percent) of them were currently unemployed; most were frequently unemployed.

The tendency to focus on psychopathology leads researchers away from potential positive uses of information gained from this population, Smith says. "Further study may help us investigate the protective factors in these women's lives, and better understand how disadvantaged women learn to cope psychologically with chronic stresses in the face of limited resources." ▲

The research was reported in the March 1993 ***Journal of Clinical Psychiatry****.*

For more information on homelessness or alcohol abuse, contact the Information Office, National Institute on Alcohol Abuse and Alcoholism, NIH, 5600 Fishers Lane, Room 16C-14, Rockville, MD, 20857, ph: (301) 443-3860. For information on drug abuse, contact the Information Office, National Institute of Drug Abuse, NIH, 5600 Fishers Lane, Room 10A-54, Rockville, MD, 20857, ph: (301) 443-1124.

Bernardine Moore is a public affairs specialist with the NIH Office of Communications.

NIH RESEARCH CAPSULES

Head Trauma, Family History, Tied to Alzheimer's Disease

Head injury in later life, especially with loss of consciousness, and a family history of dementia are significant risk factors for Alzheimer's Disease (AD), according to a study supported by NIH's National Institute on Aging, National Center for Research Resources, and National Institute of Neurological Disorders and Stroke.

While no single risk factor for the incurable brain disorder has been positively identified, some experts believe that both trauma, in particular a head injury, and genetic susceptibility may increase the likelihood of developing AD. This view is based in part on studies of professional boxers and others suffering head trauma (e.g., auto accident victims) who have developed dementia and related organic brain disorders.

To further test the hypothesis, Dr. Richard Mayeux and his colleagues at Columbia University in New York conducted a community-based study of 138 patients with AD and 193 healthy control subjects, all of whom were 65 and older. Key data to assess prevalence of head injury and family history of dementia or AD were also obtained from hundreds of relatives of both patients and controls.

The researchers found that patients with AD were 3.7 times more likely to have experienced a head injury, compared to controls. The association between AD and trauma was most apparent for those whose injury occurred after age 70. Further, the incidence of AD was greater among first-degree relatives of AD patients, but only for those whose family members had developed symptoms of dementia before age 70. The scientists found no increased risk for relatives of AD patients whose onset of illness began after age 70.

The investigators note that even among relatives of both patients and controls, head injury predicted AD independent of family history.

The research team concludes that head injury and genetic susceptibility are linked to the development of Alzheimer's Disease, which currently affects some 3 to 4 million elderly men and women.

Ref: Mayeux, R., M.D., et al., "Genetic Susceptibility and Head Injury as Risk Factors for Alzheimer's Disease Among Community-dwelling Elderly Persons and their First-degree Relatives," ***Annals of Neurology****, Vol. 33, No. 5, pp. 494-501, May 1993.*

OCD in Youth Usually Improves With Treatment, But Symptoms Can Persist

Most children and adolescents afflicted with obsessive-compulsive disorder (OCD) can expect their condition to improve significantly over time, if treated. However, symptoms may linger to a lesser degree for much of the patients' lives. The findings were reported in a carefully controlled follow-up study of OCD youth conducted by the National Institute of Mental Health. For the investigation, Dr. Henrietta L. Leonard and her colleagues reevaluated 54 pediatric

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OCD patients who had previously received clomipramine hydrochloride, the standard medication for the disorder, as well as non-pharmacological treatments such as psychotherapy or behavior therapy. Their results were compared with those obtained from young patients receiving desipramine, another antidepressant, or placebo. The reevaluation process was conducted 2 to 7 years after patients began taking clomipramine.

As a group, the clomipramine patients improved considerably when compared to baseline evaluations, and to a much greater extent than those receiving desipramine or placebo. On follow-up, during a period when 38 (70 percent) subjects were taking clomipramine, only 10 were rated worse or unchanged, but 23 (43 percent) patients still met the diagnostic criteria for OCD. Three patients were in absolute remission.

At reevaluation, 81 percent of the clomipramine patients had demonstrated at least some improvement, with nearly half rated significantly better.

OCD is characterized by chronic obsessions, intrusive or recurrent thoughts or images that are senseless, and compulsions to repeatedly perform a task, such as washing one's hands or checking door locks. About 2 percent of the general population is affected.

Ref: Leonard, H.L., M.D., et al., "A 2- to 7-Year Study of 54 Obsessive-Compulsive Children and Adolescents," **Archives of General Psychiatry**, *Vol. 50, pp. 429-439, June 1993.*

Males at Risk for Acquiring Trichomoniasis

Sexually active men are at increased risk for the sexually transmitted disease (STD) trichomoniasis. They require treatment, both to eradicate their own infection and to prevent reinfection of their partner, report scientists supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Trichomoniasis, which is caused by the parasite *Trichomonas vaginalis*, is almost always acquired through sexual contact. In women, the infection may give rise to low birthweight or premature infants, and may also increase a woman's susceptibility to the AIDS virus. The infection can also cause vaginal discharge, genital itching and irritation. While the symptoms and clinical consequences in males are less well established, it *is* known that men can transmit the disease and reinfect their sex partners even if they themselves have no symptoms.

Dr. John N. Krieger and associates at the University of Washington School of Medicine assessed the prevalence and presentation of trichomoniasis in 447, 14-to-64-year-old sexually active heterosexual males known to have been sexual partners of infected women who had been treated. One group consisted of 147 men at the STD clinic; the remaining 300 men were randomly selected by clinic file numbers.

Twenty-two percent of the men whose sex partners had trichomoniasis also tested positive for the infection.

These men were frequently symptomatic, complained of urethral discharge and had been diagnosed with urethritis (inflammation of the urethra—the tube that excretes urine from the bladder). Six percent of the randomly selected heterosexual men were infected by *T. vaginalis.*

Treatment, usually with the medication metronidazole (Flagyl, TM), can eliminate trichomoniasis, prevent reinfection of the sexual partner, and resolve symptoms.

Two to 3 million women a year have symptoms of trichomoniasis.

Ref: Krieger, J.N., M.D., et al., "Clinical Manifestations of Trichomoniasis in Men," ***Annals of Internal Medicine****, Vol. 118, No. 11, June 1, 1993, pp. 844-849, 1993.*

Evidence Indicates Chorionic Villus Sampling Is Safe

A panel of international experts has failed to find a definite link between the prenatal diagnostic technique, chorionic villus sampling (CVS), and birth defects. Although domestic studies support its safety, the panel recommended that because some safety questions about the procedure remain, pregnant women considering CVS should nevertheless be informed that there may still be an associated risk of birth defects. The panel therefore called for more studies to determine the safety of the technique.

An international review of the data following this recommendation disclosed no increase in malformations following CVS. The panel members reviewed the medical literature in a workshop sponsored by the National Institute of Child Health and Human Development (NICHD) and released its report on October 20, 1992.

CVS is one of two common prenatal, diagnostic procedures used to detect genetic defects in early pregnancy. It is usually performed in the first trimester, in contrast to the other established technique, amniocentesis, which is normally done during the second three months of pregnancy. CVS involves inserting a plastic tube through the cervix, or placing a needle through the abdomen and wall of the uterus to remove villi—thin, hairlike projections—from the placenta. Cells from the villi, which are identical to fetal cells, can then be examined for genetic abnormalities.

A few earlier studies, including several from Europe, have linked CVS to fetal malformations, in particular, shortening of the arms, legs, or the tongue. One unproven theory suggests that removing villi could cause bleeding from the placenta. In turn, this could prevent adequate oxygen from reaching the arms, legs, or tongue, causing the malformations.

Workshop participants, which included medical experts from the U.S., Canada, and Germany, were unable to determine whether CVS caused any particular kind of birth defect. Nevertheless, the participants called for additional research to investigate the CVS safety issue, and stressed that women offered the procedure be

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informed of the possible association of CVS with limb reductions and other birth defects.

In keeping with the recommendations of the conference report, further investigation into the question of CVS and limb defects has been performed. Results of the NICHD CVS and Amniocentesis Study Group have been published in the February 23, 1993 *Lancet*.

Combining recent NIH work with all other available U.S. data shows that there is no increase in the incidence of limb defects in almost 80,000 CVS cases as compared to accepted rates within the population. There were no documented cases of mouth/limb defects in the U.S. CVS experience. The conclusion of the conferees, and the evidence from the NIH and U.S. data is that the cases of limb defects following CVS from some centers may be related to trauma, especially those where the procedure was performed before 9 weeks gestation.

Ref: Report of the NICHD Workshop on CVS and Limb and Other Defects, ***Teratology****, the* ***American Journal of Obstetrics and Gynecology****, and the* ***Journal of Obstetrics and Gynecology of Canada****, July 1993.*

Panel Calls for Cigarette Tax Hikes to Discourage Youths, Poor Adults from Smoking

aising cigarette excise taxes could arkedly reduce smoking among ildren, adolescents, and low-income lults, a panel of National Cancer stitute (NCI) experts recently con- ded. The authorities believe excise es may be the most effective means top smoking among the Nation's th, yielding significant reductions in morbidity and mortality, according to the NCI summary report.

More than 8 out of 10 young people begin smoking by age 21. Nearly 3 million children and teenagers smoke cigarettes and each day 3,000 youths will begin smoking for the first time. Studies have found the earlier one smokes the more chronic the addiction becomes, and the more difficult it is to quit.

Smoking is the leading cause of preventable, premature death, but health concerns tied to smoking do not, by and large, deter young adults and children. Adult smoking rates have fallen over the past decade; adolescent rates have not. Measures to discourage youngsters from smoking are desperately needed, the experts said.

It appears that tax increases may be useful in this regard. One study noted in the panel's report showed that the impact was three times as great on youth, and had significant effects on adults as well. Similar results may occur among low-income adults. They often experience a disproportionate amount of smoking-related health consequences, and, like the youth, are also a difficult population to reach with health messages.

Based on existing evidence, the NCI panel favors significant and regular increases in tobacco excise taxes which, they say, would greatly augment smoking cessation.

Ref: ***The Impact of Cigarette Excise Taxes on Smoking Among Children and Adults—Summary Report of a National Cancer Institute Expert Panel****, Division of Cancer Prevention and Control, National Cancer Institute, August 1993.*

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MARCH 1993

NIH NEWS & FEATURES

NATIONAL INSTITUTES OF HEALTH

Depressed Stroke Patients Have a Greater Risk of Early Mortality

BY JAN EHRMAN

Patients who have suffered a cerebrovascular attack and have acute, post-stroke depression are more than three times as likely to die within 10 years than stroke patients who do not become clinically depressed. This risk appears to be even greater for depressed stroke victims who have few social contacts, according to a 10-year follow-up investigation conducted by scientists supported by the National Institute of Mental Health (NIMH).

Although the incidence of strokes has fallen dramatically over the past decade, the brain injury still strikes some 500,000 Americans annually and takes the lives of about 150,000 men and women each year. Frequently strokes cause severe physical limitations or disabilities, and there is often co-existing mental anguish, most notably depression. Data indicate that about 30 to 50 percent of stroke patients develop clinical depression and, as is true of the general population, most do not receive adequate therapy for it.

Drs. Philip L.P. Morris and Robert G. Robinson and associates from the University of Maryland in Baltimore, the Iowa College of Medicine in Iowa City, and The Johns Hopkins School of Medicine in Baltimore, looked at the effect of major depression or dysthymia (a chronic, but less severe form of depression) on mortality for 91 stroke patients whose health and mental status were tracked for 10 years following the cerebral attack. Each patient's emotional state was evaluated during the acute phase of recovery, within 3 weeks following the stroke.

Researchers found that 53 percent of the study patients died within a decade following the stroke. They also discovered that patients diagnosed with depression were nearly 3½ times more likely to have died than those whose mental state was not significantly changed following the event. This relationship was independent of other risk factors that might be associated with mortality. Further, more than 90 percent of depressed stroke patients who had few or no close social contacts, such as relatives or friends, died.

"Although our findings should be considered preliminary, they're nonetheless significant. I think they illustrate several important facts not to be overlooked," said Robinson. "First is the tremendous negative impact untreated depression can have

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JAN EHRMAN
EDITOR
301/496-2317

MARY SULLIVAN
MANAGING EDITOR
301/496-1766

RICHARD BARNES
GRAPHIC DESIGN

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on an individual's very survival, especially following a life-threatening event such as stroke. Second, we now have more evidence of the critical importance of having people around who care—social contacts. Individuals who don't have them just don't fare as well, and this becomes more evident after a health crisis or major stressful life event, as you can see from our data," he explained.

The researchers acknowledge that the findings from their study do not indicate that clinical depression, *per se*, was the absolute cause of death in the post-stroke patients; however, they believe that mental status was directly linked to health outcome. The evidence was strong enough to convince the scientists that post-stroke depression should be viewed as an independent risk factor for mortality.

Would therapeutic intervention affect survival rates? Other studies have noted a reduction in mortality for some depressed cardiac patients who received psychotherapy. Robinson is currently conducting another NIMH-funded study to examine the effect of antidepressant treatment on long-term recovery from stroke. ▲

The research was published in the January 1993 ***American Journal of Psychiatry****.*

For more information on stroke and other cerebrovascular events, contact: Information Office, National Institute of Neurological Disorders and Stroke, NIH, 9000 Rockville Pike, Building 31, Room 8A-16, Bethesda, MD, 20892; phone: (301) 496-5751.

For material on depression or other mental health disorders, contact: Information Office, National Institute of Mental Health, NIH, 5600 Fishers Lane, Room 15C-05, Rockville, MD, 20857; phone (301) 443-4513.

Jan Ehrman is editor of ***NIH News and Features****.*

Extended Use of Cardiac Drugs Benefits "At Risk" Patients

BY JAN EHRMAN

Beta-blocker drugs—medications that improve the ability of the heart to pump blood—can significantly reduce the likelihood of death in heart attack patients at high risk of future events. However, long-term use of beta-blockers offers little value for patients at lesser risk of new heart attacks or related occurrences, results of a major study supported by the National Heart, Lung, and Blood Institute indicate.

The medical community agrees that beta-blocker medications (e.g. propranolol hydrochloride, or Inderal (TM), an antihypertensive that is also used to control angina and to regulate cardiac arrhythmias) be administered to surviving heart attack patients to ease the workload of the heart and to reduce cardiovascular mortality. However cardiologists aren't certain which patients should receive the medication, and for how long.

Though the issue has been a matter of scientific controversy for more than 20 years, it still lacks a definitive answer. Resolution is crucial, however, since these drugs can elicit a number of troublesome side effects. These may include bradycardia (slowed heart beat), hypotension (low blood pressure), weakness and fatigue, insomnia, confusion, mental depression, and high blood cholesterol levels—effects that often become more prominent and deleterious after extended exposure to the medications.

To address that question, Drs. Catherine M. Viscoli, Ralph I. Horwitz, and Burton H. Singer of the Yale University School of Medicine in New Haven, CT, analyzed data from the Beta-Blocker in Heart Attack Trial (BHAT), a large, well-controlled study in which researchers enrolled heart attack patients during the years 1978 to 1980 and tracked their health status until April 1982. Clinical information was obtained on nearly 3,300 patients, both men and women 30 to 69 years of age, who were admitted to 31 medical centers in the U.S. and Canada. All patients had survived one year after entry into the trial; some were taking beta-blockers after one year, while others were not.

The researchers concluded that extended beta-blocker therapy was not beneficial for patients with low to moderate risk of death from subsequent heart disease (2,914 patients). However, in patients who had a high mortality risk based on the occurrence of events such as worsening angina, congestive heart failure, or arrhythmias in the first year following a heart attack (383 patients), "our data indicate that beta-blockers produced a 43 percent decline in the risk of death," Horwitz said.

The investigators added that patients with low to moderate mortality risk may be weaned off beta-blockers gradually after a year, but may still need to take other medications. "Decisions such as these must be made for cardiac patients on an

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> *"Our data indicate that beta-blockers produced a 43 percent decline in the risk of death."*

individualized basis and on the availability of results from carefully-controlled scientific studies such as the Beta-Blocker Heart Attack Trial. Based on our findings, how a cardiac patient fares during the first year following infarct appears to be a major factor in determining the need for continued use of beta-blockers," Horwitz concluded. ▲

This research was reported in the January 1993 ***Annals of Internal Medicine****.*

For more information on heart disease or cardiac medications, contact: Information Office, NHLBI, NIH, 9000 Rockville Pike, Building 31, Room 4A-21, Bethesda, MD, 20892; phone: (301) 496-4236.

Jan Ehrman is editor of ***NIH News and Features****.*

NIH RESEARCH CAPSULES

Radiation for Hodgkin's Disease Raises Threat of Breast Cancer in Young Women

Young women with Hodgkin's disease who receive radiation therapy, often the standard treatment, are at increased risk for breast cancer, according to a study supported by the National Cancer Institute (NCI).

To determine the risk of breast cancer, NCI grantees Drs. Steven L. Hancock and Richard T. Hoppe of the Stanford University Medical Center in California, and Dr. Margaret A. Tucker of NCI, reviewed the medical records of nearly 900 patients who were treated for Hodgkin's disease during a three-decade span (1961–1990).

The investigators found that age at irradiation and length of time following therapy proved extremely critical in determining breast cancer risk. The risk increased if patients were younger than age 30 when treatment first began, and increased even more if 15 or more years had passed since radiation therapy was administered in the young women.

As a group, Hodgkin's patients of all ages who received any type of treatment were at a fourfold increased risk for breast cancer, compared with general population rates. Hodgkin's patients treated with radiation at ages 24–29 were at seven times the risk; if younger than 15 when receiving radiotherapy, the risk for breast cancer increased by 136 times.

The findings highlight the significance of vigilant, long-term monitoring of young female patients treated for Hodgkin's disease, which strikes 7,900 Americans each year, including 3,400 females.

Ref: Hancock, S.L., M.D., et al., "Breast Cancer After Treatment of Hodgkin's Disease," ***Journal of the National Cancer Institute****, pp. 25-31, Jan. 6, 1993.*

Oral Contraceptives Increase Bone Mass After Menopause

Using oral contraceptives (OCs) for at least 6 years appears to significantly increase or maintain bone density in the lumbar spine and femoral (thigh) regions during the postmenopausal years, possibly lessening the risk of osteoporosis and its complications. The findings were reported recently by National Institute on Aging grantees.

Bone loss usually begins between the third and fourth decade. However after menopause, due to hormonal alterations, women often experience a rapid acceleration of bone loss, which may result in osteoporosis. This deleterious condition can lead to potentially life-threatening problems in older women such as spinal collapse or hip fractures. The spine, femur, hips, and wrists are primary sites for bone breakage or fractures in later life.

To assess the impact of OC use on postmenopausal bone loss, Drs. Donna Kritz-Silverstein and Elizabeth Barrett-Connor from the University of California at San Diego studied the bone mass content of 239 postmenopausal women, 55 to 69 years old. About one-third reported having used birth control pills in previous years. Twenty-one subjects took them for at least 6 years.

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Bone scanning measurements confirmed that women who used oral contraceptives (which contain estrogen) for 6 or more years had substantially greater bone density in the hip and spine, than women never using OCs. Bone mass in the wrist was not affected.

According to the investigators, these data suggest enhanced bone mineralization among the OC users. This may occur because estrogens increase calcium absorption and usually decrease calcium loss, enabling women to begin menopause with extra bone mass.

If these findings for oral contraceptives hold true in further studies, the overall public health impact could be quite significant, the scientists believe.

Ref: Kritz-Silverstein, D., Ph.D., and E. Barrett-Connor, M.D., "Bone Mineral Density in Postmenopausal Women as Determined by Prior Oral Contraceptive Use," **American Journal of Public Health,** *Vol. 83, pp. 100-102, Jan. 1993.*

Depressed Elderly Benefit from Combined Treatment—Medication and Psychotherapy

Nearly 4 out of 5 elderly patients placed on the tricyclic antidepressant nortriptyline (Pamelor, TM) while undergoing psychotherapy achieved full remission of their depression within 9 weeks of therapy, and maintained their improved health status with 16 weeks of maintenance treatment. These findings are preliminary results of a clinical trial supported by the National Institute of Mental Health (NIMH).

The study, conducted by Dr. Charles F. Reynolds III and his colleagues at the University of Pittsburgh School of Medicine, involved 73 elderly patients (60 to 80 years old, three-fourths were women) with recurrent major depression. They underwent an initial 9 weeks of the combined nortriptyline/counseling therapy, followed by a 16-week regimen of nortriptyline along with biweekly psychotherapy sessions.

Of 61 subjects who completed the initial stage of the trial, 48 (78.7 percent) achieved full remission, and 3 obtained partial remission; depressive symptoms did not improve for 10 of the participants. Under placebo-controlled, double-blind conditions, none of the 24 patients maintained on nortriptyline relapsed, while 6 of 25 randomly assigned to placebo suffered a relapse.

The researchers believe that the study demonstrated that depressed elderly patients benefit from combined treatment at a success rate similar to other age groups. Further, the study shows that discontinuing drug treatment, especially during the early stages of the disorder, raises the risk for relapse in the aging population.

Ref: Reynolds, C.F., III, M.D., et al., "Combined Pharmacotherapy and Psychotherapy in the Acute and Continuation Treatment of Elderly Patients With Recurrent Major Depression: A Preliminary Report," **American Journal of Psychiatry,** *Vol. 149, No. 12, pp. 1687-1692, Dec. 1992.*

Antiviral Rx Offers Long-Term Management of Recurrent Fever Blisters

The antiviral drug acyclovir (Zovirax, TM) can markedly reduce the chronic outbreaks of cold sores and promote quicker healing in those plagued by the painful mouth blisters, say researchers at the National Institute of Dental Research (NIDR) and National Institute of Allergy and Infectious Diseases (NIAID).

In a first-of-its-kind investigation which involved 56 otherwise healthy patients studied at the NIH's Clinical Center in Bethesda, MD, NIDR's Dr. James F. Rooney and colleagues assessed the value of using acyclovir on individuals who suffered from repeated episodes of fever blisters (herpes labialis). For the study, some subjects took 400 milligrams twice a day for four months, while others received placebo. The patients then were switched to the alternate treatment.

Results indicated that acyclovir decreased episodes of cold sores by 53 percent. Further, patients receiving the medication took about 4 days to attain complete healing of the herpes infection, while those taking placebo took nearly twice as long to heal.

Approximately one-third of the U.S. population suffers from fever blisters, accounting for nearly 100 million episodes each year. One out of 10 of these individuals suffers 6 or more outbreaks a year. Symptoms of recurrent cold sores may be either mild or painful.

Although long-term use of acyclovir is effective, it should not be routinely recommended for all patients with recurrent fever blisters. The medication should probably be reserved for those who suffer the most from the condition since the drug must be taken daily, has potential side effects, and is costly, according to Rooney.

Ref: Rooney, J.F., M.D., et al., "Oral Acyclovir to Suppress Frequently Recurring Herpes Labialis. A Double-Blind, Placebo Controlled Trial," ***Annals of Internal Medicine****, Vol. 118, No. 4, pp. 268-272, Feb. 15, 1993.*

Clinical Eye Info Reliably Obtained Via Phone Interviews

Can visual acuity be accurately assessed over the telephone? Results of a unique, National Eye Institute-funded study suggest that it can indeed be accomplished, and with a high degree of reliability.

Dr. Ronald Dei Cas and his co-researchers at the Georgetown University School of Medicine in Washington, DC, evaluated the visual acuity of 89 patients by conducting a telephone interview that involved the participant's use of a home eye test. The test kit included a string attached to a patch to be placed over one eye. When extended, the other end of the string displayed a reading card containing test numbers of various sizes on several lines. The apparatus was designed to be strapped around the back of the head.

All subjects, generally healthy men and women 20 to 88 years of age, were previously scheduled to receive ophthalmologic exams in an eye clinic within several weeks of taking the telephone test.

Upon comparison, the telephone interviews and the clinical exams agreed in 91 percent of cases on a near

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vision test, and in 86 percent of tests on a more distant line of vision.

Phone interviews are a practical, reliable, and cost-effective method for determining visual acuity in large populations, and may be especially useful in testing individuals least likely to seek regular ophthalmologic exams, say the investigators.

Ref: Dei Cas, R., M.D., et al., "Assessment of Visual Acuity Via a Telephone Interview," **Archives of Ophthalmology**, *Vol. 110, pp. 1279-1282, Sept. 1992.*

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JANUARY/FEBRUARY 1994

NIH NEWS & FEATURES

NATIONAL INSTITUTES OF HEALTH

High Vitamin E Intake May Help Thwart Colon Cancer

BY JAN EHRMAN

Adding to the growing body of evidence on the beneficial effects of vitamin E, scientists supported by NIH's National Cancer Institute (NCI) have recently determined that large, supplemental amounts of the antioxidant may help prevent colon cancer, especially in women under age 65.

Colon cancer is the second leading cause of cancer death in the United States. It is not known, specifically, what causes the disease, but dietary factors have been implicated.

The recent findings were gleaned from a comprehensive study of thousands of women participating in the Iowa Women's Health Study Cohort, part of a larger NCI-funded prospective study of breast cancer.

"Surprisingly, perhaps, ours is one of the few investigations to assess the independent effects of vitamin E on the development of colon cancer," says Dr. Roberd M. Bostick, the lead researcher from the University of Minnesota in Minneapolis.

Vitamin E, or alpha-tocopherol, is an antioxidant (protective substance) found in foods such as sunflower seeds, nuts, leafy green vegetables, and some vegetable oils. Since many individuals consume very little dietary vitamin E, in some cases less than the recommended daily allowance (RDA) of 30 international units (IU), some people believe that supplements may be useful. Anticipating its benefits, consumers have begun augmenting their diets with the vitamin for its potential protective edge against cancer and heart disease.

Besides vitamin E, vitamin C, beta-carotene (a vitamin A derivative), and some minerals are also antioxidants. These nutrients help protect the body against destructive substances such as free radicals, which may transform a cell from normal to cancerous. Vitamin E and the other antioxidants appear to trap or neutralize the activity of free radicals, and thus may be useful in cancer prevention. In an earlier study, NCI scientists reported a link between vitamin E consumption and lowered oral cancer risk (Gridley, et al., *American Journal of Epidemiology*, May 15, 1992).

Can vitamin E also thwart or at least delay the onset of colon cancer, a disease that took the lives of more than 48,000 Americans in 1991? The answer appears to be yes, according to the University of Minnesota researchers.

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JAN EHRMAN
EDITOR
301/496-2317

RICHARD BARNES
GRAPHIC DESIGN

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Bostick and his colleagues investigated whether large amounts of antioxidants, including vitamin E, had an impact on the development of colon cancer among 35,000 women, aged 55–69. The scientists reviewed the subjects' dietary questionnaires which provided information on food intake, and vitamin and mineral use. In a retrospective review of the participant's health records, they cited 212 cases of colon cancer that had developed during the 5-year follow-up period. The researchers discovered that those who had developed colon cancer reported significantly lower intakes of vitamin E (dietary and supplemental E combined) than women who remained free of the disease.

"After adjusting for age, we found a strong link between vitamin E and the incidence of colon cancer," says Bostick. "Most notably, we saw a big jump in the *decrease* of colon cancer at a daily intake of just 30 IUs." "Further," he added, "the risk decreased progressively as the amount of vitamin E intake increased." The effects were most apparent in women younger than 65.

How does vitamin E suppress colon cancer? There are several intriguing theories, according to the researcher. As noted, antioxidant micronutrients such as vitamin E may shield against cell-damaging free radicals, but the vitamin may also stimulate and enhance the immune system to attack budding cancer cells. Finally, says Bostick, vitamin E may inhibit the production of nitrosamines, byproducts of nitrites which are used as common food preservatives. Nitrosamines have been shown to cause tumors in lab animals and, in large amounts, may do the same in humans, experts believe.

Despite the research team's findings, Bostick stops short of saying that everyone, even persons with risk factors for colon cancer (e.g., a family history of the disease) should be consuming supplemental vitamin E. "It would be nice to make that recommendation. And although we now have animal as well as some epidemiological evidence to support it, it's still a little early," he contends.

In the meantime, however, the researcher/physician strongly encourages individuals to bolster their intake of vitamin E-rich foods, and also to follow a low-fat, high-fiber, high-vegetable-and-fruit diet, and get regular physical activity, measures which themselves may minimize the risk for developing colon cancer. ▲

This study was published in the September 15, 1993 issue of ***Cancer Research****.*

For more information on cancer, contact: Information Office, National Cancer Institute, NIH, 9000 Rockville Pike, Building 31, Room 10A-18, Bethesda, MD, 20892, phone: (301) 496-5583.

Jan Ehrman is editor of ***NIH News and Features****.*

New Contraceptive Vaccines Target Both Men and Women

BY ROBERT BOCK

Investigators funded by NIH's National Institute of Child Health and Human Development (NICHD) are studying ways to create vaccines that would destroy sperm or eggs, or otherwise prevent fertilization. These scientists met recently with others in the field to describe their progress.

"Since the advent of oral contraceptives, few new contraceptives have been introduced to the U.S. market," said Dr. Nancy J. Alexander, Chief of the Contraceptive Development Branch of NICHD's Center for Population Research. "Because most women have diverse requirements during their reproductive lives, the availability of a variety of methods is important."

"...the availability of a variety of (contraceptive) methods is important."

Many of the studies reported at the meeting involve research on sperm and egg antigens. Part of the body's normal defense system, antigens are substances—usually foreign—that stimulate the production of antibodies which then bind to the antigens, targeting them for eventual destruction by the cells of the immune system. Scientists hope that by injecting them into the body, the antigens on sperm and eggs will produce antibodies and eventually prevent fertilization.

Much of the research has been on identifying possible antigens on the sperm head. Key proteins targeted for vaccine research have been those involved directly with the sperm's binding to the egg or with fertilization.

Such studies have already begun in female baboons and have resulted in high levels of antibodies against specific sperm antigens, Alexander said. Although most of the animals become infertile, Alexander explained that a few still retain their fertility, apparently because they fail to manufacture the appropriate antibodies. Researchers at NICHD's three university Contraceptive Development Centers hope to overcome this problem by developing a polyvaccine containing several different sperm antigens.

"The idea is that if several proteins are used, more individuals will develop an immune response," Alexander said.

She added that it is important to test possible contraceptive antigens thoroughly, to make sure that they do not provoke an immune response in other organs of the body.

Other researchers have developed a contraceptive vaccine for men against the key male reproductive hormone, luteinizing hormone releasing hormone (LHRH). The investigators have completed animal studies on LHRH safety and effectiveness, and will now test the vaccine in healthy human male volunteers.

NICHD scientists are also developing a contraceptive vaginal ring. Preliminary clinical trials indicate that, although the device delivers one-third less hormone than conventional oral contraceptives, it is as effective and nearly free of side effects. ▲

For more information on contraceptives, contact: NICHD, ph: (301) 496-5133.

Clues to Mobility Problems Explained by Animal Research

BY SUZANNE M. LEWIS

The loss of brain receptors—specifically, those that normally enable the brain chemical dopamine to regulate motor control—appears to be responsible for certain mobility deficits seen in normal aging, animal studies show. These deficits may include impaired balance, posture, and gait, according to scientists at the National Institute on Aging's Gerontology Research Center (GRC) in Baltimore, MD.

To a lesser degree, the decrements observed in the aging rodents mimic those seen in individuals afflicted with such neurological disorders as Huntington's disease and Parkinson's disease—incapacitating illnesses that hamper the body's ability to move and effectively coordinate movements.

In the case of motor control, proper communication between cells that both make and receive dopamine is critically essential.

The key players governing movement are the neurotransmitters and receptors. Neurotransmitters, such as dopamine, are brain chemicals that act as messengers, sending key signals or messages to one another. Neurotransmitters latch on to receptors—proteins that lie on the surface of healthy nerve cells, or neurons. In order to facilitate communication between neurons, both neurotransmitters and receptors must be present. In the case of motor control, proper communication between cells that both make and receive dopamine signals is critically essential.

A study conducted by Dr. George S. Roth and his colleagues at the GRC found that as animals age, there is a progressive decline in the quantity of one class of dopamine receptor known as D_2. D_2 receptors play a vital role in motor control. One reason for the decline is cellular—some nerve cells die as a part of normal aging, which accounts for about 50 percent of the receptor loss. Death of the other half occurs at the molecular level where there is less messenger ribonucleic acid (mRNA), which is needed to produce dopamine receptors. Roth and his research team are the first scientists to explain why there are lowered levels of dopamine receptors in older animals.

To learn how the molecular mechanism for age-related loss of dopamine receptors works, the GRC investigators extracted nuclei from nerve cells in the corpus striatum of young and old rats. The corpus striatum is an area of the brain that contains receptors that receive dopamine. The scientists then added the building blocks for mRNA to the nuclei and observed the rate of production for mRNA. Roth and his co-researchers found that the striatal nuclei from old rats produced only 40 to 50 percent of the mRNA for the D_2 receptor, when compared to levels observed in young rats. The rate at which this mRNA was produced in the nuclei of surviving brain cells was decreased 20–25 percent.

This research appears to confirm earlier studies suggesting that there are specific alterations in gene expression associated with aging. (Gene expression occurs when a gene is "turned on," or activated, thus enabling the gene to deliver

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vital instructions to a cell). Now for the first time, GRC investigators are able to offer an explanation for impairments in physiological control mechanisms—namely, that during normal aging, decreased mRNA production for dopamine receptors accounts for the decline in motor control.

"I am optimistic and very encouraged by our results," said Roth. "Further pursuit into this area may someday point the way towards effective treatments for debilitating neurological ailments such as Huntington's and Parkinson's disease, while enhancing our understanding of normal human aging," he concluded. ▲

This research was published in the Volume 17, 1993 issue of ***Molecular Brain Research****.*

For more information on aging, contact: Information Office, National Institute on Aging, NIH, 9000 Rockville Pike, Building 31, Room 5C-27, Bethesda, MD, 20892; phone (301) 496-1752, or the Information Office, NIA Gerontology Research Center, 4940 Eastern Avenue, Room 1-D-15, Baltimore, MD, 21224, phone (410) 558-8114.

Suzanne Lewis is a public affairs specialist with the GRC.

NIH RESEARCH CAPSULES

Saliva-Producing Agent Abets Dry Mouth in Cancer Patients

Patients suffering from dry mouth, often the result of irradiation for head and neck cancer, may benefit by taking pilocarpine, a drug that stimulates saliva production, according to the results of a large multicenter clinical trial that included researchers with NIH's National Institute of Dental Research (NIDR).

Oral dryness is a frustrating and potentially serious side effect of radiation therapy, which is given to many of the 43,000 patients who each year are diagnosed with head and neck cancer. Also known as xerostomia, dry mouth can produce considerable oral discomfort and pain, tooth decay, mouth infections or ulcerations, and may make chewing, speaking, and swallowing difficult. The effects are usually permanent. Besides radiotherapy, dry mouth may also be the result of certain disorders, most notably Sjogren's syndrome (an autoimmune disease), medications, a nutritional deficiency, anxiety or depression, or damage to the nerves that stimulate the salivary glands.

In this study, Dr. Jonas T. Johnson of the University of Pittsburgh Medical Center and colleagues, along with Drs. Philip C. Fox and Ingrid H. Valdez of the NIDR, assessed the effects of pilocarpine or placebo (a look-alike, inactive pill) on 166 patients who completed a 12-week, double-blind, placebo-controlled trial. All patients suffered from dry mouth as a result of radiation for head and neck cancer, but each participant had at least one partially functioning salivary gland, a requisite for pilocarpine to be effective. Subjects, all of whom were randomly selected for treatment, were administered either 5 mg. of pilocarpine, 10 mg. of the drug, or placebo, three times a day at mealtimes. Neither the investigators nor the patients knew which treatment was being given.

Results indicated that 54 percent of participants receiving 5 mg. of pilocarpine reported symptomatic improvement of the mouth and tongue, while 44 percent of those taking 10 mg. of the medication also reported a decrease in oral dryness. Symptoms decreased progressively as the study progressed, and most patients reported the maximum improvement at the end of the 12 weeks.

Side effects from pilocarpine were for the most part minimal, and usually limited to increased sweating.

The fact that pilocarpine helped boost saliva production even at relatively low dosages is encouraging, the researchers contend, particularly since taken at high doses the drug can cause increases in heart rate and blood pressure.

*Ref: Johnson, J.T., M.D., et al., "Oral Pilocarpine for Post-Irradiation Xerostomia in Patients With Head and Neck Cancer," **New England Journal of Medicine**, Vol. 329, pp. 390-395, August 1993.*

Light Treatments Help Elderly "Make It Through the Night"

Carefully timed exposures of bright light may lead to a better night's rest for some older men and women, according to a study conducted by scientists supported by the National Institute of Mental Health (NIMH).

While some older people report difficulty falling asleep, a more common complaint among the aged is sleep maintenance, that is, the ability to remain asleep until morning. Because of this problem, many obtain a poor overall quality of sleep, in some cases experiencing early morning awakenings (EMAs), which can result in drowsiness and other problems during the day.

Dr. Scott S. Campbell and associates at the Cornell University Medical College in White Plains, New York studied the efficacy of using bright light exposure in the treatment of sleep maintenance problems among a group of healthy individuals, 62–81 years of age. All subjects had been experiencing EMAs for at least one year prior to the investigation. For the study, participants received 2-hour *bright* light treatments for 12 consecutive evenings. Control subjects received similarly timed exposures of *dim* light.

The researchers found that as a whole, treatment considerably enhanced sleep efficiency among study participants. On average, bright light therapy reduced waking time (total time spent awake after having initially fallen asleep) in these subjects by one hour (reduced from 102.8 minutes to 43.2 minutes awake), most notably during the last two-thirds of the night. Further, the number of awakenings declined in those receiving bright light—from 25 episodes a night to less than 15 awakenings a night, following therapy. Total sleep time was increased by 45 minutes in the group. No such improvements were observed in the control subjects.

Although sleep efficacy was significantly enhanced using bright light exposure, future studies may help determine if longer exposures would further reduce the number of minutes spent awake. Investigators will also assess whether *less* frequent (and thus more convenient) treatments (e.g., twice a week) would elicit similar therapeutic benefits.

About half of all older adults suffer from sleep-related problems.

Ref: Campbell, S.S., Ph.D., et al., "Alleviation of Sleep Maintenance Insomnia with Timed Exposure to Bright Light," ***Journal of the American Geriatrics Society****, Vol. 41, pp. 829-836, Aug. 1993.*

Second-Hand Smoke Causes Early, Accelerated Development of Arterial Plaque

Animal studies conducted by scientists supported by NIH's National Institute of Environmental Health Sciences add further evidence of the damaging effects of sidestream cigarette smoke. In young cockerels (roosters), relatively modest exposure to second-hand smoke led to early, yet significant plaque formation in the abdominal aorta. In humans, plaque formation augments the risk for heart problems.

Drs. Arthur Penn and Carroll A. Snyder of the New York University Medical Center in Tuxedo, NY, exposed

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30 very young cockerels to sidestream cigarette smoke for 6 hours a day, 5 days a week for 16 weeks. Twelve age-matched roosters inhaled filtered air for the same time interval. All animals were fed low-cholesterol diets. Both groups of cockerels were later studied to assess plaque formation in the abdominal aorta, the abdomen's main artery.

Microscopic examinations of the two groups of animals showed that inhalation of sidestream smoke produced significant increases in the size of plaques or blockages that had developed in the abdominal aortas of the smoke-exposed cockerels. This increase did not occur in the control animals.

The investigators note that cockerel and human arteriosclerotic plaques are structurally similar. With this in mind, and based on study findings, the scientists conclude that moderate exposure to sidestream smoke, even for brief periods early in life, may accelerate arteriosclerotic plaque development in young children.

It is estimated that as many as 40,000 heart-related deaths occur annually due to involuntary breathing of second-hand cigarette smoke. Sidestream smoke can also be dangerous for children and adults with asthma or other chronic respiratory ailments.

Ref: Penn, A., PhD, and C.A. Snyder, PhD, "Inhalation of Sidestream Cigarette Smoke Accelerates Development of Arteriosclerotic Plaques," **Circulation**, *Vol. 88 (part 1), pp. 1820-1825, Oct. 1993.*

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NIH NEWS & FEATURES

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More "Oldest Old" on the Horizon, But Agreement on Longevity Ends There, Say Experts

BY JAN EHRMAN AND VICKY CAHAN

Today, men and women 85 and older—about three million—are the most rapidly growing age group in the U.S., according to the National Institute on Aging (NIA). And as of 1990, more than 35,800 Americans were 100 years of age or beyond.

But can each of us realistically expect to live that long? Will our children experience such good fortune?

Expert opinions vary considerably and many were shared at a recent workshop on forecasting life expectancy, funded by the NIA. While disparate views were offered at the event, one general point of agreement came through loud and clear—the years ahead will bring forth a greatly expanded cluster of the "oldest-old"— men and women age 85 and beyond. Still, just how many individuals will become members of this unique population, and whether life's limits can reasonably be extended beyond 85, remain open for debate.

Average life expectancy has risen dramatically over time, note demographers. At the turn of the century, the average American could expect to live to 47 years. Today, a child born in 1993 can anticipate surviving almost 60 percent longer—to around 75 years. Census Bureau estimates show that about one out of every 100 youngsters born between 1979 and 1981 will reach the heralded century mark.

The issue of longevity and lifespan has long fascinated poets and perplexed gerontologists—scientists who study the clinical, biological, social, and psychological processes of aging. Some gerontologists espouse the theory that senescence is commandeered by a biological clock, one that is programmed to cease ticking at a certain time despite man's best efforts to intervene.

Dr. James Vaupel of Odense University Medical School in Denmark, however, is far more optimistic. He believes that average life expectancy at birth will indeed surpass the biblical four score and seven years. NIH, he said at the workshop, will be at the forefront in finding ways to make this possible. Furthermore, he maintains that many current life expectancy estimates—that average life expectancy will reach 85 years—are far too conservative because advances in treating leading killers, such as coronary heart disease and cancer should keep people living

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JAN EHRMAN
EDITOR
301/496-2317

MARY SULLIVAN
MANAGING EDITOR
301/496-1766

RICHARD BARNES
GRAPHIC DESIGN

longer. "The work of NIH is going to pay off and there are going to be breakthroughs that extend life expectancy up to 90 or 100 years," predicted Dr. Vaupel.

The prediction is based in part on Dr. Vaupel's most recent investigation which shows that the upper limits to life may be much higher than previously believed. In an article published in the October 16, 1992 issue of *Science,* he and his colleagues reported that in their study of a particular population of more than a million Mediterranean fruit flies, once the insects reached senescence, their statistical likelihood of dying decreased, not increased, as most experts believe happens with aging. Dr. Vaupel and other authorities now strongly suggest the same phenomenon could be true for humans. Even modest advances in longevity of 10 or 11 years "will produce huge increases in the estimated numbers of very old people," explained Dr. Richard Suzman, director of NIA's Office of the Demography of Aging. He cited Census Bureau projections that in 50 years there will be more than 12 million people age 85 and over. "However, there are others who predict that we'll have from 23 million to 40 million," Dr. Suzman added.

Recent mortality figures offer some additional cause for optimism. According to Dr. Kenneth Manton of Duke University, death rates for those 85 and older declined 8.7 percent between 1988 and 1991. Additional declines can be anticipated in the ensuing years, other experts contend.

While genetic manipulation and breakthrough technologies to lengthen life may be years or even decades away, the NIA maintains that currently there are no known 'antiaging' treatments, drugs, or supplements that retard aging or prolong life. Nevertheless, by following prudent measures such as exercising regularly, getting sufficient rest, refraining from smoking, maintaining proper body weight, and obtaining periodic medical checkups, men and women can bolster their chances for getting more years out of their life.

For more information on life expectancy and aging, contact: Information Office, NIA, NIH, 9000 Rockville Pike, Building 31, Room 5C-27, Bethesda, MD, 20892; phone: (301) 496-1752.

Jan Ehrman is editor of ***NIH News and Features.*** *Vicky Cahan is a public affairs specialist with NIH's National Institute on Aging.*

NIMH Prevention Program Helps Women Change AIDS Risk Behavior

BY CAREE VANDER LINDEN

Women at risk for HIV infection reported greater AIDS knowledge, increased condom use, and fewer unsafe sexual practices just 3 months after participating in a behavioral intervention program supported by the National Institute of Mental Health (NIMH).

Within 3 months, these women increased their condom use by 40 percent, significantly reduced occurrences of unprotected intercourse, and stopped having sex with intravenous drug users, according to lead researcher, Dr. Jeffrey A. Kelly of the Medical College of Wisconsin.

The findings were collected from the first 92 subjects to complete the controlled study of 250 women in an urban health care clinic in Milwaukee.

Inner-city women with multiple or high-risk partners, or a history of sexually transmitted diseases are at notably high risk for HIV. The NIMH-funded study is one of the first to evaluate the impact of AIDS education for this population.

Based on the responses of the women during initial interviews, "we learned that the best recruitment strategies for an AIDS risk program with this group should focus on the child and family values that are most important to these women, such as: protect your child from AIDS; protect your unborn infant from AIDS; and stay healthy in order to care for your children," Kelly said. Participants learn basic information about AIDS and HIV, including how the virus is transmitted, which behaviors make them vulnerable to infection, and how they can protect themselves.

They also learn and practice skills such as condom use and assertiveness.

"Many AIDS interventions focus on techniques such as how to apply a condom," said Kelly. "That's important, but we're also trying to focus on the reasons these women should protect themselves—not just on the methods."

One particularly difficult issue for such women is how to negotiate safer sex practices in an ongoing relationship without the partner becoming insulted and ending the relationship. "We use group sessions to try to prepare the women for resistance from their partners," explained Kelly. "We focus on helping them to get out of relationships where they cannot change the high- risk behavior and teaching them the skills needed to introduce safer sex practices in new relationships."

As the women develop rapport during the group sessions, they encourage each other to try out the behavioral change at home. At the following session, participants share their experiences.

Kelly has noted a strong sense of mutual support among women in the intervention groups. "We are teaching skills, but the real power is in what they learn through group interaction. These women—many of whom have little control over other aspects of their lives—are helping each other prepare for change." ▲

> *"...We learned that the best recruitment strategies for an AIDS risk program with this group should focus on the child and family values that are most important to these women..."*

For additional information about AIDS and high-risk behavior, contact: Information Office, NIMH, NIH, 5600 Fishers Lane, Room 15-105, Rockville, MD, 20857; phone: (301) 443-4513.

Caree Vander Linden is a public affairs specialist with NIH's National Institute of Mental Health.

Cardiac Patients at Risk with "Desirable" Total Cholesterol, But Low HDLs (When Too Little Good is Bad)

BY JAN EHRMAN

Heart disease patients with desirable levels of total cholesterol, but insufficient amounts of "good" blood fats, known as HDL (high density lipoprotein) cholesterol, are at a dangerously elevated risk for future heart attacks and other cardiovascular events, according to a National Heart, Lung, and Blood Institute-supported study.

High blood cholesterol is a primary risk factor for atherosclerosis and coronary artery disease (CAD), this country's leading killer. Well over 7 million people in the U.S. are afflicted with CAD. Excessive blood cholesterol has been tied to an unhealthy diet, smoking, hypertension, and perhaps, to a lesser degree, a sedentary lifestyle. Genetics is also often a contributing factor.

A complete lipid analysis should be obtained in all heart disease patients, regardless of total serum cholesterol, in order to screen for low HDL.

When measured, blood fats can be isolated into several distinct components including total cholesterol, HDL or high density lipoproteins, and LDL, low density lipoproteins. High amounts of HDL cholesterol are considered protective, since HDL removes excess cholesterol from tissues and transports it to the liver where it is ultimately excreted in bile. If HDL is low and LDL is high, cholesterol accumulates in the bloodstream and body tissues, where it can clog the coronary arteries and restrict blood flow. Angina and/or damage to the heart muscle as occurs during myocardial infarction may result, especially during periods of exertion when more oxygen-rich blood is needed by the heart.

Dr. Michael Miller and his colleagues from The Johns Hopkins Medical Institutions and the University of Maryland Medical Systems, both in Baltimore, and the Mary Imogene Bassett Research Institute in Cooperstown, NY, conducted a follow-up study in which they evaluated 107 middle-age adults who were diagnosed with CAD in the late 1970s to determine what factors predicted new cardiovascular events over a 13-year period.

All patients, 83 men and 24 women with an average age in the mid-50s, demonstrated desirable levels of total serum cholesterol, that is cholesterol less than 200 mg/dL (milligrams per deciliter of blood). Some, however, had low HDL concentrations while others had greater amounts.

The investigators' objective was to determine if a low HDL level was an independent risk factor for future cardiovascular events in the heart patients, despite the presence of acceptable amounts of total cholesterol. What they discovered has profound clinical implications.

"A low level of HDL proved to be a strong predictor of recurrent cardiac events for this group," said Miller. During the 13 years the patients were followed, he pointed out, 75 percent of those with low HDL cholesterol (less than 35 mg/dL) died from a heart attack or experienced a second myocardial infarct or unstable angina that ultimately resulted in cardiac surgery, while fewer than half of subjects with higher HDL levels did.

Medical experts have previously acknowledged that low HDL levels, even among healthy individuals, can elevate the likelihood of cardiovascular problems. Some earlier investigations in cardiac patients have even demonstrated that raising the HDL lessened this risk. But these patients did not have normal or desirable concentrations of total blood cholesterol.

"Our investigation was different in that we assessed heart disease patients whose total blood fats were within normal limits. Based on this determination, it might have appeared they were safe," said Miller. But the researchers' findings didn't support this, not if the patients' HDL was also depressed, he explained. "What it tells us is that you could easily gain a false sense of security if you merely examined total serum cholesterol in these patients. That's obviously not enough," the clinician added.

The results of Miller's study suggest that a complete lipid analysis be obtained in all heart disease patients, regardless of total serum cholesterol, in order to screen for low HDL. If HDL levels are found low (less than 35 mg/dL), some efforts can be made to alter them including exercise, smoking cessation, estrogen supplementation (for women), and if needed, certain cholesterol-altering drugs. Raising HDLs often proves challenging, however. While diet and weight control frequently reduce total and LDL cholesterol, weight loss often modestly *lowers* HDLs. A drop of one point in HDL increases the risk of a heart attack by about 3 percent.

Before treatment recommendations for low HDL cardiac patients can be offered with assurance, larger studies are needed to determine if raising the favorable cholesterol in this population will significantly reduce future cardiovascular events, say the scientists. ▲

This research was published in the October 1992 issue of *Circulation*.

For more information on cholesterol and heart disease, contact: Information Office, NHLBI, NIH, 9000 Rockville Pike, Building 31, Room 4A-21, Bethesda, MD, 20892; phone: (301) 496-4236.

Jan Ehrman is editor of ***NIH News and Features.***

NIH RESEARCH CAPSULES

Maintenance Drug Therapy Prevents Recurrent Depression

Remaining on the antidepressant drug imipramine for more than 3 years continues to ward off bouts of recurrent depression in patients who previously responded to the tricyclic agent, according to a small study conducted by National Institute of Mental Health grantees. Tricyclics are often the first drug of choice in treating depressive episodes, but the medication is sometimes discontinued once the acute depressive phase has abated.

Dr. David Kupfer and his colleagues at the University of Pittsburgh School of Medicine conducted a placebo-controlled, double-blind study of the efficacy of maintenance imipramine for patients with a history of recurrent depression. All 20 patients previously benefited from a 3-year trial with the antidepressant.

Only one patient receiving imipramine during the 2-year study experienced a depressive recurrence (researchers suspect he was taking the medication improperly), whereas two-thirds of subjects (6 of 9) receiving placebo did.

Based on these findings, the investigators conclude that imipramine's prophylactic effects apparently last beyond 3 years. They further recommend that patients who have suffered repeated episodes of depression less than 2½ years apart should probably remain on this or a similar maintenance antidepressant for at least 5 years.

Ref: Kupfer, D.J., M.D., et al., "Five-Year Outcome for Maintenance Therapies in Recurrent Depression," ***Archives of General Psychiatry****, Vol. 49, pp. 769-773, 1992.*

Selenium Blocks Colon Cancer in Lab Animals

An investigation of rodents conducted by National Cancer Institute grantees provides additional support for the role of dietary selenium in inhibiting colon tumor development and growth.

A connection between cancer of the colon and selenium deficiencies has become apparent in recent years. Epidemiologists have determined that rates for colorectal cancer are high in geographical areas where selenium is in short supply.

Further, earlier studies demonstrated a link between selenium and the prevention of colon cancer, when the inorganic form (sodium selenite) was added to the drinking water or diets of rats. Although inorganic forms of selenium have been shown to deter colon cancer, their toxicity is of concern.

For the present study, Dr. Bandaru S. Reddy and his associates from the American Health Foundation in Valhalla, NY, synthesized a less toxic, organic form of selenium and investigated the effects of adding small and larger amounts of it to a high-fat diet 2 weeks before (initiation stage), during, and up to 3 days after (post initiation) cancer was induced in young rodents. Control animals ate a standard high-fat diet, free of additional selenium.

The researchers found that supplemental selenium had significant tumor-inhibiting effects in the colon during both the initiation and post initiation stages. Control animals showed no such benefits—tumors developed and proliferated as anticipated.

Selenium is found naturally in some vegetables, cereals, and grains. Despite its potential for prophylaxis in humans, selenium supplements should be viewed with caution since the substance, taken in larger amounts than those obtained from foods, may be toxic.

Ref: Reddy, B.S., Ph.D., et ol., "Chemoprevention of Colon Corcinogenesis by the Synthetic Orgonoselenium Compound 1,4-Phenylenebis(methylene)selenocyonote," **Concer Research**, *pp. 5635- 5640, Oct. 15, 1992.*

Study Shows Reinfection of Hepatitis C Possible; Vaccine Hopes Wane

Aspirations for a vaccine for hepatitis C have been dimmed with the recent finding that reexposure to the virus does not protect against reinfection. This conclusion was reached by National Institute of Allergy and Infectious Diseases researchers in their investigation of chimpanzee blood specimens.

Hepatitis C virus (HCV) is a global phenomenon that can affect all socioeconomic classes in both developing and developed countries. In the U.S., HCV is linked to 20 percent of all clinical hepatitis cases. More than half of all people exposed to the virus become carriers and up to 20 percent of carriers develop cirrhosis, a severe liver disease. In the U.S., intravenous drug users make up about 30 percent of the HCV-infected population. Experts contend that nearly all IV drug users are ultimately infected by the potentially lethal virus. HCV may also be acquired through sexual contact and to a far lesser extent, blood transfusions.

Drs. Patricia Farci and Robert Purcell of the NIAID and their coresearchers conducted a retrospective analysis of specimens obtained from five chimpanzees that over a 3-year period had been reinoculated with the same or different strains of HCV, some up to four times. They found that reinfection occurred several times in the animals that were rechallenged with different HCV strains, as well as in one chimp rechallenged with the same dose of the original virus.

According to the scientists, when natural protection against infection by closely related viruses or the same virus on rechallenge cannot be demonstrated, "then prospects for vaccine development become somewhat bleak."

Ref: Forci, P., M.D., et ol., "Lock of Protective Immunity Agoinst Reinfection with Hepotitis C Virus," **Science**, *Vol. 258, pp. 135-140, Oct. 2, 1992.*

Animal Model Proposed for Obsessive-Compulsive Disorder

Investigators at the National Institute of Mental Health (NIMH) have demonstrated that the canine licking disorder known as acral lick dermatitis (ALD) may be an appropriate animal model for studying the psychiatric condition obsessive-compulsive disorder (OCD). This revelation may help usher in new

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therapeutic modalities for this affliction, which affects about 2 percent of the population.

OCD is characterized by persistent, troublesome thoughts, as well as excessive cleaning, grooming, and "checking" behaviors—for example, frequent hand-washing or repeatedly checking the stove or door locks. Earlier studies conducted by Rapoport and others showed that serotonin-uptake inhibitor drugs such as clomipramine hydrochloride were somewhat effective in curbing symptoms of OCD. Serotonin is a chemical or neurotransmitter that helps brain cells communicate.

ALD, which most often affects large species of dogs such as German shepherds and Great Danes, occurs when the animals chronically lick their paws or flanks to the point where they become ulcerated and often infected.

Dr. Judith Rapoport and her NIMH colleagues conducted three double-blind crossover comparisons of several different types of drugs—including several that block serotonin uptake (clomipramine, desipramine, and fluoxetine). The research team then compared responses from the three drugs to those obtained from a tricyclic antidepressant and a placebo—neither of which affected serotonin. The research was conducted on 42 dogs.

The investigators found that the three serotonin uptake drugs were clinically effective in reducing chronic licking in the dogs, but not the placebo or the antidepressant. The behavioral similarities expressed between ALD and OCD, as well as the likeness of drug responses in the canines and human subjects suggest that canine ALD may serve effectively as an animal model for OCD.

Ref: Rapoport, J.L., M.D., et al., "Drug Treatment of Canine Acral Lick: An Animal Model of Obsessive-compulsive Disorder," Archives of General Psychiatry, *Vol. 49, pp. 517-521, 1992.*

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NIH NEWS & FEATURES

NATIONAL INSTITUTES OF HEALTH

Kegel Exercises Help Kids Overcome Bedwetting, Incontinence

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BY JAN EHRMAN

Training children in the Kegel technique—simple exercises which strengthen the pelvic muscle—can help eliminate or greatly reduce episodes of both daytime and nighttime urinary incontinence, report researchers funded by NIH's National Institute of Mental Health.

"Kegel is an uncomplicated, easy-to-learn technique that now appears to have very broad applications, not only for adults, but now we find also for children who suffer from daytime incontinence or bedwetting. Many kids and their parents agree that these can be very frustrating and disturbing problems," says Dr. Richard S. Surwit of the Duke University Medical Center in Durham, NC, a scientist in the study.

Urinary incontinence, the inability to control urination, affects 3 to 4 percent of children between 4 and 12 years of age. Besides the psychologic consequences of incontinence, the involuntary bladder contractions which trigger urge incontinence (the inability to hold urine long enough to reach a toilet), the most prevalent type in children, often promote urinary tract infections (sometimes due to the stagnant urine left behind in clothing, which enables bacteria to travel up the urethra.)

While certain medications, behavioral techniques, and other approaches (e.g., urine alarms, sound-emitting devices that wake the child from sleep when he or she begins to lose urine) have reduced bouts of wetting for some youngsters, a simple, non-invasive, cost-effective procedure with widespread usefulness has long been needed, child health experts agree. Researchers have known for some time that bladder retraining exercises such as the Kegel technique can help control some types of incontinence in adults, however there is little information on its applicability in youth.

Surwit, along with colleagues Drs. Mark S. Schneider and Lowell R. King, evaluated the use of the Kegel technique to treat (daytime) urinary incontinence in 79 children, primarily girls, with an average age of 7½ years. The procedure was also used to treat the nearly two-thirds (52) of these children who also experienced nighttime wetting, some of whom were as old as 15.

Each youth received an average of less than 2 total hours of Kegel training, which consisted of instructions on how to tighten the pelvic muscles and hold the

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EDITOR
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contraction for 5 to 20 seconds. They were also taught to use the procedure to stop urination in mid-stream before resuming, which also helps strengthen the pelvic muscles. The youngsters were encouraged to practice this routine often throughout the day.

According to the researchers, within 2 months, 47 (60 percent) of the children were completely cured of daytime incontinence. The incessant urge to void was also eliminated. Eleven (14 percent) of the children had a partial reduction in both urinary incontinence frequency and urgency. Twenty-one children did not benefit from treatment.

The Kegel technique, which can easily be taught by most health care professionals, also significantly helped nearly three-quarters of the children who also experienced nighttime wetting—a clinically valuable finding since this technique has never before been used for nocturnal enuresis, or "bedwetting."

"What we think happens (via the Kegel technique) is that the procedure inhibits the involuntary bladder contractions, which in turn decreases the child's relentless urge to void. At the same time, this very likely increases bladder volume (the amount of urine the bladder can hold), which further enables the youngster to hold their urine until they can reach the bathroom," explains Surwit.

"More studies need to be done to confirm what we've found and to fully understand the mechanisms that are operating, however based on our results, we feel confident in prescribing the Kegel technique for several types of childhood urinary incontinence, including bedwetting," says Surwit. For many children, he concludes, it could provide a welcome relief, eliminating the need for medications or other, more complex, sometimes physically invasive therapies that parents and kids alike would prefer to avoid. ▲

This research was published in the January 1994 issue of ***Pediatrics****.*

For more information on this research, contact the NIH's National Institute of Mental Health (301) 443-4513. For general information on incontinence, call the NIH's National Institute on Aging, (301) 496-1752, and the NIH's National Institute on Diabetes and Digestive and Kidney Diseases (301) 496-3583. For information on bedwetting, contact the NIH's National Institute of Child Health and Human Development (301) 496-5133.

Jan Ehrman is editor of ***NIH News and Features****.*

Depression Linked to Smoking Cessation Among Older Women

BY JAN EHRMAN

For the first time, scientists report that older female smokers who are also depressed are four times more likely to "kick the habit" than their non-despondent peers. Researchers from the NIH's National Institute on Aging (NIA) and the Duke University Medical Center conducted the long-term study, which involved thousands of individuals.

"What this means is that we have to rethink the way we address the issue of smoking and depression, at least in older women," says NIA's Dr. Marcel E. Salive, an epidemiologist and the lead scientist in the study. "We can no longer make the blanket statement that depression provides a *barrier* to smoking cessation."

> *"We can no longer make the blanket statement that depression provides a barrier to smoking cessation."*

Most investigations on smoking and mental health have involved adolescents or middle-aged men and women. These studies have generally shown that depression predisposes to smoking initiation, and that despondent smokers have more difficulty quitting than non-depressed smokers. Until now, however, the issue of smoking and depression and how they interact in an older population has been virtually ignored.

Salive, and Dr. Dan G. Blazer of the Duke University Medical Center in Durham, North Carolina, used data from a longitudinal study which involved nearly 4,000 elderly (65 and older) North Carolina residents to examine the impact of depression upon smoking cessation rates. Following initial interviews, three annual follow-up investigations were conducted.

At the time of the initial interview (baseline measurement), nearly 15 1/2 percent of the participants smoked. According to a clinical assessment scale, depression was highest among current smokers (11.2 percent), while 9.5 percent of never smokers were clinically depressed. A little over 7 percent of former smokers met the diagnosis.

Three years later, among women who first scored high on the scale for depression, 55 percent had "kicked the habit," while only 25 percent who scored lower for depressive symptoms had done so. On the other hand, older depressed men were slightly *less* likely to have quit smoking than age-matched, male smokers who were not depressed.

"I must admit, I was somewhat surprised by the findings with the women," says NIA's Salive. They virtually negate the commonly-held assumption that nicotine may serve as a form of self-medication for depression, at least in older women, he adds.

Why are elderly, depressed female smokers more likely to relinquish cigarettes than women of the same age who are not depressed? No one knows for sure, but Salive suspects that the depression may be somehow motivating these individuals

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to quit. A definitive answer may emerge from future studies, he says.

In the meantime, the researcher emphasizes that the findings should compel clinicians to extend their efforts to encourage their elderly, depressed female patients to quit smoking. "What it tells us is that physicians should not give up on the depressed smoker. A little extra effort could go a long way here," says Salive. "Whatever the reason, we now believe that these women are quite amenable to treatment or encouragement that will enable them to put down their cigarettes once and for all." ▲

This study appeared in the December 1993 ***Journal of the American Geriatrics Society****.*

For more information on smoking and aging, contact the NIH's National Institute on Aging, (301) 496-1752, and the National Heart, Lung, and Blood Institute, (301) 496-5343. To obtain material on depression and aging, contact the NIH's National Institute of Mental Health, (301) 443-4513, and the National Institute on Aging.

Jan Ehrman is editor of ***NIH News and Features****.*

Space Flight May Spawn Health Problems

BY JAN EHRMAN

Astronauts face potentially detrimental changes in their physiology that may impact on their health, especially during take-offs, landings, and as a result of long periods of space travel, said Dr. Arnauld Nicogossian of the National Aeronautics Space Administration (NASA).

Nicogossian reported these findings at a recent Clinical Grand Rounds Lecture held at the National Institutes of Health in Bethesda, MD.

Some physiological changes that take place during space flight mimic those often seen in aging, including bone loss, atrophy of muscle tissue, blood pressure fluctuations, and elevation of heart rate, said the NASA scientist. Dental problems, kidney stones, gastrointestinal disorders, and (space) anemia frequently arise during or as a result of space voyage, especially for astronauts who remain in flight for a month or more. Space anemia occurs because fewer red blood cells are needed, and thus, fewer are produced in the absence of gravity. This finding has important health implications for long-term space flight.

Space anemia occurs because fewer red blood cells are needed, and thus, fewer are produced in the absence of gravity.

As a result of these changes, numerous health threats and medical dilemmas exist, both in space and after landing, explained Nicogossian. For example, during flight, blood pressure may fluctuate significantly, although it is difficult to obtain reliable blood pressure measurements. Also, due to the absence of gravity, the central nervous system does not receive the needed cues to properly orient itself. As a result, motion sickness is common.

After returning to earth, space travelers may encounter additional obstacles, for example with walking and estimating distances. Additionally, about a third of these individuals undergo heart rate and blood pressure abnormalities which may become permanent.

NASA scientists are working with NIH investigators to study changes in bone, muscle tissue, and hormones during space flight. While attempting to prevent space-related abnormalities and stabilize body functions, they will also investigate medical treatments to determine if specific therapies, as applied on earth, can be utilized for space flight illness or injury. Presently, there are no solid data on the effects of long-term space flight on health. ▲

*Jan Ehrman is editor of **NIH News and Features**.*

NIH RESEARCH CAPSULES

Cholesterol-Lowering Drug Topples Blood Fat Levels in Postmenopausal Women

Low doses of lovastatin (Mevacor, TM), a cholesterol-lowering medication, can help safely and effectively reduce damaging blood cholesterol in postmenopausal women, according to a well-controlled study supported by the National Heart, Lung, and Blood Institute. In particular, the drug increased the quantity of low-density lipoprotein (LDL) receptors, which help remove LDL cholesterol, the harmful form of cholesterol that clogs arteries and can lead to coronary heart disease.

On average, cholesterol levels tend to rise in women as they complete menopause and lose estrogen. Most of the total cholesterol increase occurs in the form of LDL, which can accumulate inside arterial walls and cause vessel narrowing (atherosclerosis). Before menopause, a woman's risk for coronary heart disease is less than that of a man's. However, postmenopausal women, particularly those not receiving supplemental estrogen, are at comparable risk for a heart attack or other cardiac event to their male counterparts.

This study, conducted by Drs. Marcello Arca, Gloria Lena Vega, and Scott M. Grundy at the University of Texas Southwestern Medical Center and the VA Medical Center in Dallas, was two-phased. First, the scientists investigated the metabolic mechanisms responsible for high blood cholesterol in 39 women, 26 with high cholesterol, and 13 controls with normal cholesterol. The second part of the study, involving 16 postmenopausal women, was placebo-controlled so that neither the investigators nor the randomly selected subjects knew if they were taking lovastatin or the inert substance. After eight weeks, all of the women were crossed over to the alternate regimen.

Results from the first phase showed that hypercholesterolemia (high blood cholesterol) in women was primarily due to a lack of LDL receptors. Findings from phase 2 documented that lovastatin, at doses of only 10 mg. a day, safely and effectively lowered blood cholesterol, both total cholesterol and LDL. On average, the drug decreased total blood cholesterol from 272 mg/dL. (milligrams per deciliter of blood) to 221, and caused LDL amounts to drop from an average 171 mg/dL. to 134.

When dietary changes prove ineffective, the researchers say, low-dose lovastatin provides a reasonably safe, useful treatment for enhancing blood cholesterol profiles in postmenopausal women.

Ref: Arca, M., M.D., et al., "Hypercholesterolemia in Postmenopausal Women. Metabolic Defects and Response to Low-Dose Lovastatin," ***Journal of the American Medical Association****, Vol. 271, No. 6, pp. 453-459, Feb. 9, 1994.*

Fish Oil May Help Reduce High Blood Pressure

Data from studies of more than 1,300 subjects indicate that supplementary fish oil can help modestly reduce blood pressure in hypertensive individuals, those with elevated blood cholesterol, and persons with heart disease. The analysis was performed by scientists supported by NIH's National Institute of Environmental Health Sciences.

Although a number of studies have been carried out to evaluate the effects on blood pressure from a high-fish diet or fish oil supplements, the results have been inconsistent. Still, some experts suspect that the fatty acids in fish oils, known as omega-3s, could elicit a hypotensive (blood pressure-lowering) effect for some individuals.

To determine if such a cause and effect exists, Dr. Martha Clare Morris and her associates from the Harvard School of Public Health, Brigham and Women's Hospital and Harvard Medical School in Boston analyzed 31 previously conducted, placebo-controlled investigations involving 1,356 participants. This review included all studies that reported the effects of fish oil on blood pressure using two criteria—a placebo control, and blood pressure measurements both before and after the trials. The trials lasted from 3 to 24 weeks.

Although fish oil produced no change in the blood pressure of healthy subjects, the data overwhelmingly suggested that the oil moderately lowered blood pressure in the majority of subjects with hypertension, elevated blood cholesterol, and cardiovascular disease. Larger amounts of fish oil generally produced greater declines in blood pressure than smaller amounts. Very low supplemental dosages generated virtually no effect.

While the findings are important, due to the very large dose of fish oil (more than 10 capsules a day) required to produce a moderate decrease in blood pressure (3–4 mm Hg), the investigators believe that fish oil supplements are *not* a practical therapy for hypertension.

Ref: Morris, M.C., et al., "Does Fish Oil Lower Blood Pressure? A Meta-Analysis of Controlled Trials," ***Circulation****, Vol. 88, No. 2, pp. 523-533, Aug. 1993.*

Caffeine Consumption Impairs Female Fertility

Moderate caffeine intake, such as amounts from drinking three cups of coffee a day, can lower a woman's likelihood of conceiving by as much as 27 percent. Even smaller amounts can slightly reduce her chances of becoming pregnant, report researchers funded by NIH's National Institute of Child Health and Human Development and the National Institute on Drug Abuse.

Little is known about the biologic underpinnings of delayed conception or infertility, while even less solid data are available on the association between caffeine intake and female reproduction.

Two former NIH-supported scientists—Drs. Elizabeth E. Hatch, previously with the Yale University School of Medicine in New Haven, CT and now a researcher with NIH's National Cancer Institute, and Michael B. Bracken—interviewed 1,909 women during early

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pregnancy to ascertain if a link existed between caffeine consumption and fertility. Following the first prenatal visit, the women were queried about the length of time taken to conceive, and were also asked to give approximations of daily caffeine intake from coffee, tea, and soft drinks.

The investigators found that women consuming 300 milligrams of caffeine daily (the equivalent of 3 cups of coffee) had a 27 percent lower chance of conceiving per menstrual cycle, compared to caffeine abstainers. Even moderate or modest caffeine consumption reduced the ability to conceive. Women drinking the equivalent of 1 to 2 cups of coffee a day lowered their likelihood of becoming pregnant by about 10 percent.

The researchers aren't certain why caffeine would inhibit or delay conception, however one hypothesis is that the substance may directly affect ovulation by producing changes in hormone levels (e.g., reduced estrogen), which would lessen the chance to conceive.

Meanwhile, although caffeine appears to be associated with reduced or delayed fertility, the scientists look to future studies to determine whether another substance found in caffeinated beverages may actually be the offending agent.

Ref: Hatch, E.E., Ph.D., and M.B. Bracken, Ph.D., "Association of Delayed Conception with Caffeine Consumption," ***American Journal of Epidemiology,*** *Vol. 18, No. 12, pp. 1082-1093, 1993.*

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JULY 1994

NIH NEWS & FEATURES

NATIONAL INSTITUTES OF HEALTH

Scientists Uncover New Link Between Obesity and Immunity

BY JAN EHRMAN

Researchers supported by NIH's National Cancer Institute (NCI) have shown that there may be more health risks to obesity than previously thought. Obesity may alter the immune system and could thus create a vulnerability to certain diseases, including cancer.

Experts unanimously agree about the health risks of being extremely overweight. Obesity, which reflects an imbalance between caloric intake and expenditure, affects about one in four American adults. The disorder can hinder longevity, and is a well-established risk factor for a number of potentially serious medical problems.

While the injurious effects of obesity may not strike until the adult years, it is thought that some clinical manifestations of the problem may originate in childhood or adolescence. Recently scientists at the New York Hospital-Cornell Medical Center assessed whether 40 obese adolescents, ranging in age from 9–17 years, demonstrated evidence of altered immune function.

Funded by NCI, Dr. Susanna Cunningham-Rundles and her colleagues investigated the influence of obesity on various elements of immunity in the markedly overweight, but otherwise healthy adolescents—24 females and 16 males, with an average age of 13.6 years.

Looking at one particular element, the investigators assessed the effects of obesity on Tumor Necrosis Factor (TNF) in the adolescents. Small amounts of this substance help promote wound healing and may fight certain tumors. But when TNF is produced suddenly in larger, uncontrolled quantities, a potentally lethal shock syndrome occurs. This happens, for example, in septic shock resulting from blood poisoning.

TNF in larger amounts has been implicated as the cause of wasting in some cancers, and similarly, the wasting associated with AIDS. Recent studies in genetically obese rodents have shown that TNF may also play a pivotal role in insulin resistance, a smaller than expected response to insulin. Earlier studies established a strong link between insulin resistance and obesity. In the genetically obese rodents, TNF production was greatly increased.

The reasons obesity is closely related to insulin resistance (and diabetes) are as yet poorly understood. Insulin regulates glucose (carbohydrate) metabolism, while

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adipose (fat) tissue, where energy is stored, is an insulin responsive tissue. Insulin resistance as shown in the obese animal studies, is directly related to increased TNF production by the fat cells.

In a landmark finding taken from the current study, Cunningham-Rundles and associates found that blood cells of obese adolescents secrete large amounts of TNF spontaneously, while cells of normal weight teens do not. They discovered that TNF status was linked to degree of obesity even among obese subjects. The researchers found further that the most obese subjects had the highest spontaneous TNF production, just like the genetically fat mice and rats. These patients were all found to be insulin resistant.

"This is a critically important finding. What it tells us is that there is a very close link between the regulated level of TNF and insulin resistance. This is the first time it's been demonstrated in humans. It precisely indicates that the relationship between obesity and TNF is *much* closer than we thought," explains Cunningham-Rundles. She adds, "Before this we thought that being obese caused potentially unhealthful immune changes, but we had no idea that the immune system could directly affect metabolism."

The researcher says that the next step is to verify these findings and to determine whether there is a genetic basis for high TNF levels, the outcome of which could determine the individual's therapeutic options. For example, she explains, "If there is a genetic susceptibility to having high TNF, then increasing the amount of exercise, while it may cause weight loss, probably won't affect TNF." Some other treatment would be needed to mediate TNF levels and ultimately influence obesity, Cunningham-Rundles concludes. ▲

This research was published in Vol. 699 of the ***Annals of the New York Academy of Sciences****, 1993.*

For information on cancer and immunity, contact NIH's National Cancer Institute, ph: (301) 496-5583. To receive information on obesity, contact NIH's National Institute of Diabetes and Digestive and Kidney Diseases, ph: (301) 496-3583.

Jan Ehrman is editor of ***NIH News and Features****.*

NIH RESEARCH CAPSULES

Smoking Greatly Augments Stroke Risk in Men

In the largest prospective study ever conducted to evaluate the link between cigarette smoking and stroke, NIH-supported scientists have found that men who smoke a pack of cigarettes a day more than double their risk of stroke. However, quitting smoking almost entirely eliminates this risk, say the researchers, who were funded by NIH's National Heart, Lung, and Blood Institute and NIH's National Cancer Institute.

While cigarette smoking has been firmly linked to stroke in some studies, other investigations have suggested only a small association. Some others have not established a cause and effect relationship at all. Some of these studies, however, lacked control subjects, which may have affected the accuracy of the data.

Drs. Anthony S. Robbins and colleagues from Brigham and Women's Hospital, Harvard Medical School, and the Harvard School of Public Health in Boston examined data obtained from more than 22,000 healthy, male doctors, aged 40–84 years, participating in the Physicians' Health Study, directed by Dr. Charles H. Hennekens. This was a randomized, double-blind, placebo-controlled trial of aspirin and beta-carotene usage initially designed to determine the effects of these substances on the incidence of cancer and cardiovascular disease.

The participants originally answered a lengthy questionnaire describing, among many other items, their use of cigarettes. The men were then followed for an average of nearly 10 years. After controlling for other stroke risk factors, such as alcohol intake, current smokers of 20 or more cigarettes a day were found to have 2 ½ times the risk of having a stroke, compared to men who had never smoked. Those currently smoking fewer than 20 cigarettes daily were at double the risk, while former smokers were at an average 1.2 times the risk for stroke, compared to men who had never smoked.

The investigators conclude that cigarette smoking is a major risk factor for stroke and stroke-related deaths and disability. More than 500,000 nonfatal strokes and 145,000 fatal strokes occur in the U.S. each year.

Ref: Robbins, A.S., M.D., MPH, et al., "Cigarette Smoking and Stroke in a Cohort of U.S. Male Physicians," ***Annals of Internal Medicine****, Vol. 120, No. 6, pp. 458-462, March 15, 1994.*

Low-Fat Diet Deters Development of Skin Tumors

Trimming dietary fat can help reduce the incidence of actinic keratosis—a common, premalignant skin tumor, say researchers funded by NIH's National Cancer Institute (NCI).

Actinic keratoses are sun-induced skin growths which, if left untreated, can turn into skin cancer. Keratoses frequently affect persons 60 years and older, but younger individuals are also susceptible.

Animal studies have previously demonstrated that dietary fat can have an adverse effect on sun-induced skin cancers. In addition, excess caloric intake may also promote tumor initiation and growth in animals. But little is known about the effect of diet on tumors, including actinic keratoses, in humans. This issue was examined by Dr. Homer S. Black and his colleagues from the VA Medical Center and the Baylor College of Medicine, both in Houston, TX.

For the study, 76 middle-aged patients (52 men, 24 women) with non-melanoma skin cancer were randomly assigned to one of two groups: a control group whose diet was not changed, or an intervention group that was instructed to alter their diets so that no more than 20 percent of total calories were consumed as fat. At four month intervals for the following 24 months, all subjects were examined by their physicians (who were unaware of their dietary regimen) for the presence of new keratoses.

On average, control subjects, all of whom were consuming at least 36 percent of their calories as fat, were diagnosed with new keratoses about 4 times as often as individuals in the low-fat group.

Based on these findings, say the researchers, a low-fat diet may now be considered useful for preventing actinic keratosis.

Ref: Block, H.S., Ph.D., et al., "Effect of a Low-Fat Diet on the Incidence of Actinic Keratosis," ***The New England Journal of Medicine****, Vol. 330, pp. 1271-1275, May 5, 1994.*

Benefits of Neuroleptic Drug Extend to Many Schizophrenic Patients

In the first study of its kind, NIH's National Institute of Mental Health (NIMH) investigators have determined that clozapine (Clozaril, TM), a drug used successfully to reduce schizophrenic symptoms in severely ill, treatment-resistant patients, appears to have much broader applications—it may also ease symptoms in less ill, community-dwelling schizophrenic men and women.

One of the most important advances in research on schizophrenia, a complex and difficult-to-treat mental disorder, has been the development of clozapine, which belongs to the class of drugs known as atypical neuroleptics. A number of studies have documented clozapine's superior ability to reduce schizophrenic symptoms (e.g., hostility, hearing disturbing or threatening voices, delusions) in the most seriously affected, often hospitalized individuals, many of whom did not benefit from other neuroleptics or experienced adverse side effects when taking them. Various investigations have demonstrated improvement on behavioral measures by as much as 60 percent for patients taking clozapine. Meanwhile, experts wonder whether the medication could provide similar gains for less seriously ill, chronic schizophrenic outpatients. This was the focus of a well-controlled study conducted by NIMH's Dr. Alan Breier and scientists at the University of Maryland School of

Medicine in Baltimore.

The researchers compared the effects of clozapine to another neuroleptic, haloperidol, for reducing symptoms in 19 and 20 outpatient schizophrenic patients, respectively, who had partially responded to other chemically-related drugs. For this study, neither the patients nor the investigators knew which treatments patients were receiving. The trial lasted 10 weeks.

Results demonstrated that clozapine was far superior to haloperidol in reducing many schizophrenic symptoms, including hostility. In addition, the drug produced few adverse reactions. Clozapine's major side effect is agranulocytosis, a somewhat rare, but potentially fatal blood disorder. Patients who take clozapine require weekly blood tests to monitor for this reaction.

Based on this study's findings, the researchers believe that clozapine may be a valuable treatment for a large number of chronic schizophrenia outpatients, helping many of these moderately symptomatic individuals avoid institutionalization.

Ref: Breier, A., M.D., et al., "Effects of Clozapine on Positive and Negative Symptoms in Outpatients With Schizophrenia," ***American Journal of Psychiatry****, Vol. 151, No. 1, pp. 20-26, January 1994.*

Risk Factors Identified for Nasal Cancer

Cigarette smoking, inhaling second-hand smoke, drinking alcohol, and an improper diet can increase the risk for developing nasal cancer, according to National Cancer Institute (NCI) scientists studying data from nearly 600 individuals. On the positive side, frequent consumption of vegetables lowered the risk.

Replicating findings from earlier investigations, the NCI researchers also found that working at certain jobs, especially those in the woodwork or textile industries, also magnified nasal cancer risk by at least 60 percent.

To conduct their investigation, Drs. Wei Zheng, Joseph K. McLaughlin and their NCI associates analyzed data from the 1986 National Mortality Followback Survey, a National Center for Health Statistics (NCHS) study which included a representative sample of one percent of deaths in the U.S. among persons aged 25 years or older. Data were obtained from the records of 147 white males who died from nasal cancer and 449 control subjects who died from other causes.

In assessing potential risk factors for nasal cancer, the researchers determined that men who had ever smoked were 20 percent more likely to develop nasal cancer, compared to those who had never smoked. This risk increased with the number of cigarettes smoked, as well as the length of time the individual smoked. An effect for the inhalation of second-hand smoke was also noted. Among nonsmokers, men with nasal cancer were 3 times more likely to have had wives who smoked than men who did not have nasal cancer.

Diet also played a role, the data revealed. Drinking alcohol increased the likelihood of developing nasal cancer. Regular consumption of salted/

smoked foods also elevated the risk for the disease, while frequent consumption of vegetables lowered the risk.

Carcinoma of the nasal cavity and surrounding areas is relatively rare compared to other forms of cancer. Nevertheless in 1989, the latest year for which figures are available, 502 Americans died from nasal cancer and carcinomas of the sinuses and middle ear, according to the NCHS.

Ref: Zheng, W., M.D., J.K. McLoughlin, Ph.D., et al., "Risk Factors for Cancers of the Nasal Cavity and Paranasal Sinuses among White Men in the United States," ***American Journal of Epidemiology****, Vol. 138, No. 11, pp. 965-972, 1993.*

Estrogen May Help Ward Off Cataracts

A survey of nearly 5,000 middle-aged to elderly women suggests that estrogen may offer modest protection against cataracts. These findings were reported by scientists supported by NIH's National Eye Institute.

Researchers know that estrogen, the principal hormone in females, affects the body in many different ways, although few studies have specifically focused on estrogen's effects on the eyes. Dr. Barbara E. Klein and her associates from the University of Wisconsin Medical School in Madison assessed the possible link between supplemental estrogen use and the presence of lens opacities (cataracts) in 4,926 women, 43 to 84 years old, all previous participants in the Beaver Dam Eye Study. All subjects participated in medical interviews, which included the gathering of significant information on menopausal status. These were followed by medical tests, including among other things, ophthalamic exams and photographs of the lenses of the eyes.

After adjusting for factors that might contribute to clouding of the lens, such as alcohol intake and cigarette smoking, the scientists found a correlation between estrogen exposure and lower prevalence and severity of cataracts. They found that women who began menstruating at a younger age and those who reached menopause at an older age—thus exposed to estrogen longer—also had lower cataract risk. Paradoxically, it appears, women who had complete hysterectomies had *less* severe stages of nuclear sclerosis (a certain type of cataract) than did other women; however in many cases these individuals were taking supplemental estrogen, say the researchers.

Future investigations should help determine whether estrogen inhibits the development of cataracts, or whether other factors are responsible for the protective effect observed in this study.

Ref: Klein, B.E.K., M.D., et al., "Is There Evidence of an Estrogen Effect on Age-Related Lens Opacities? The Beaver Dam Eye Study." ***Archives of Ophthalmology****, Vol. 112, pp. 85-91, Jan. 1994.*

Doc's Postcard Prompts Women to Obtain Mammography

Women are twice as likely to go for a mammogram when they are sent a reminder postcard after an initial mailed recommendation, conclude researchers funded by NIH's National Cancer Institute (NCI). They also found that having the correspondence signed by their personal physician has virtually no additional effect.

Despite its proven value in detecting even very small, non-palpable breast tumors, mammography is underutilized. Data indicate that as of 1990, only one-third of women had ever obtained more than one mammogram. Many approaches to increase screenings have been attempted, including mailed recommendations, but the results have been inconsistent, and experts aren't sure which approach works best.

Dr. Stephen H. Taplin of the Group Health Cooperative of Puget Sound, Seattle, WA, and his associates randomized 1,500 women, age 50–79, into four correspondence groups: women who received a letter from their doctor; women who received both a letter and a postcard from their doctor; those who received a letter and a reminder postcard from Group Health's Breast Cancer Screening Program director; and a control group who received only a letter from the program director. All correspondence recommended that women call and schedule an appointment for a program visit, which included a mammogram.

The scientists found that while the physician's personalized letter did not influence whether women sought mammography, the reminder postcard, when sent within 2 months of the initial letter, nearly doubled the likelihood that the women would obtain a mammogram within one year. The probability of screening also doubled if the women had previously had a mammogram.

Risk factors which reduced by half the likelihood of obtaining mammography included being in fair or poor health, smoking, or using primary care offices located more than 45 minutes from the screening center.

Postcard reminders effectively encourage women to seek mammograms when preceded by a letter recommending they schedule an examination, conclude the scientists.

Ref: Toplin, S.H., M.D., MPH, et ol., "Using Physicion Correspondence ond Postcord Reminders to Promote Mommogrophy Use," ***American Journal of Public Health****, Vol. 84, No. 4, pp. 571-574, April 1994.*

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NIH NEWS & FEATURES

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Megadose Vitamins May Lessen Risk of Recurrent Bladder Cancer

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BY JAN EHRMAN

In what appears to be a major advance in the treatment of urological cancers, researchers in a double-blind trial supported in part by NIH's National Cancer Institute (NCI) have shown that large, supplemental amounts of vitamins along with zinc can halve the risk of recurrent bladder cancer.

"We were quite surprised by these findings—so much in fact that at first we didn't believe them," said the principal researcher, Dr. Donald L. Lamm, of the West Virginia University School of Medicine in Morgantown. "We rechecked our findings and literally could not believe how good the results were," he told *NIH News and Features.*

More than 50,000 people in the U.S. are diagnosed each year with carcinoma of the bladder, according to the NCI. Caucasians run twice the risk of blacks, and men are afflicted 2 to 3 times as often as women. While the disease predominantly affects persons 55 years or older, young people may also be stricken. Cigarette smoking and working in certain occupations such as manufacturing and textiles may heighten the likelihood of developing bladder cancer, but other factors are probably also involved, most experts maintain.

Despite the fact that malignant tumors of the bladder can often be surgically removed before they spread, the cancers nevertheless return in nearly 9 out of 10 patients. Evidence has hinted that vitamin supplementation may help in the prevention of certain cancers, perhaps even recurrent cancer of the bladder, but few clinical trials have been conducted thus far.

For the current study of 65 bladder cancer patients, Dr. Donald L. Lamm and his co-researchers assessed the value of using megadose vitamin supplements, along with zinc, in combination with standard therapy known as bacillus Calmette-Guerin (BCG), to determine whether this regimen could halt bladder tumor recurrence. BCG is a relatively new form of biological therapy in which scientists use natural or laboratory-made substances to stimulate the cancer patient's immune system to arrest disease more effectively. BCG was administered directly into the bladder of these patients.

One group of patients received BCG therapy plus oral vitamin supplements meeting only the recommended daily allowance (RDA). Meanwhile, the other

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JAN EHRMAN
EDITOR
301/496-2317

RICHARD BARNES
GRAPHIC DESIGN

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group was given the BCG, the RDA multivitamins, plus an additional 40,000 units of vitamin A, 100 mg. of vitamin B6, 2,000 mg. of vitamin C, 400 units of vitamin E, and 90 mg. of zinc. (Lamm cautions that some types of vitamin A, when taken in large amounts, can be toxic. The water soluble type however, is not stored in the liver and is not considered harmful). These amounts far exceed the RDAs. For example, the RDA for vitamin C is 60 mg, vitamin E, only 30 mg. Patients and physicians were both unaware which therapy each group received.

Findings revealed that after 10 months following these protocols, the megadose supplements appeared to help prevent tumor recurrence. Cancer returned in only 40 percent of those in the group receiving the larger supplement amounts, while 80 percent of patients in the control (RDA) group experienced tumor recurrence.

Further studies may help elucidate, specifically, which substances are responsible for the antitumor effects. "I think there is probably more than one mechanism of action responsible for the prevention of new tumors. It could be the antioxidant effect the vitamins conferred." (Antioxidants are protective substances which help neutralize the activity of free radicals—naturally-produced chemicals that can damage body cells.) "It could also relate to a reduction in urinary carcinogens (cancer-causing substances such as nitrosamines) from the vitamin B6, the vitamin C, or the vitamin E," Lamm speculated. Or, he added, it may have to do with stimulation of the immune system, since each of the four vitamins given do have a positive effect on immune function. "It may have brought about an increase in natural killer (NK) cells." NK cells normally have the ability to destroy budding cancers.

Regardless of the operating mechanism, with positive findings in hand, Lamm has since placed all of the bladder cancer patients from his study on the vitamin regimen. "Naturally we're very pleased with our findings. Now we hope to promptly confirm them through a larger, multicenter trial," the investigator said.

In the meantime, Lamm and other experts urge cancer patients to continue following their prescribed treatments and avoid megadose vitamin therapy unless so advised by their physician. ▲

This study was published in the January 1994 issue of ***The Journal of Urology.***

NIH RESEARCH CAPSULES

Long-Term Drug Therapy Helps Bulimic Patients

A minimum of six months of drug therapy is required for patients with the eating disorder bulimia nervosa to achieve significant improvement, say researchers funded by NIH's National Institute of Mental Health (NIMH).

Bulimia nervosa, a psychiatric condition that predominantly strikes young women, is characterized by episodes of binge eating (repetitive eating of large amounts of food over a short time) followed by purging (self-induced vomiting or excessive use of laxatives or diuretic drugs to lose weight). These incidents may range from once or twice a week to several times a day. As with the related eating disorder anorexia nervosa (self-starvation with dramatic weight loss, and a distorted body image), the medical consequences can be devastating. About 10 percent die from their eating disorder.

While cognitive-behavioral therapy (CBT), a psychological treatment approach taken either by itself or in combination with antidepressant medication, has been shown to help bulimic patients in the short run, few trials have tracked these individuals for as long as one year after treatment was initiated.

In this one-year follow-up study of 61 female bulimia patients (18–65 years old) randomly assigned to one of five treatment groups, Dr. W. Stewart Agras and associates from the Stanford University School of Medicine in California found that patients receiving CBT, either by itself or combined with the antidepressant desipramine for at least 24 weeks, experienced far greater reductions in binge eating than patients taking desipramine for only 16 weeks. Specifically, better than 75 percent of patients who received 24 weeks of treatment were free of binge eating and purging at follow-up, as compared with only 18 percent of those taking desipramine for 16 weeks.

The researchers conclude that desipramine, either alone or in combination with CBT, should be continued for at least 24 weeks.

Larger trials would help verify the importance of sustained therapy for resolution of bulimic symptoms, note the scientists.

*Ref: Agras, W.S., M.D., et al., "One-Year Follow-Up of Psychosocial and Pharmacologic Treatments for Bulimia Nervosa," **Journal of Clinical Psychiatry**, Vol. 55, No. 5, pp. 179-183, May 1994.*

Mutating Hepatitis C Virus Dodges Immune System

The elusive hepatitis C virus (HCV) cleverly sidesteps the human immune system by swiftly mutating, before ultimately damaging the liver. This finding, drawn from a study led by scientists at NIH's National Institute of Allergy and Infectious Disease (NIAID) obscures hopes for developing a fully effective HCV vaccine.

Experts believe that as many as 5 million people worldwide are infected with HCV. It is thought that as a result about half have or will develop chronic liver inflammation. Nearly one in five persons with chronic hepatitis C develop cirrhosis, a condition that can lead to liver cancer. Risk factors for HCV include receiving a contaminated blood transfusion and sharing needles with infected persons. It is not clear whether the virus may also be transmitted sexually.

The research was conducted by Drs. Patrizia Farci and Robert H. Purcell along with their NIAID colleagues, in conjunction with scientists from the NIH Clinical Center in Bethesda, MD, Georgetown University in Washington, DC, and Bioqual, Inc., in Rockville, MD. Results of the investigators' work showed they prevented HCV infection in one chimpanzee who received a mixture of an HCV strain taken from a patient stricken with post-transfusion hepatitis and plasma containing potentially neutralizing antibodies obtained from the same patient two years later, when he was chronically infected with HCV.

In contrast, antibodies obtained from the same patient in 1990 (11 years later) could no longer neutralize HCV when the mixture of virus and antibodies was given to two chimpanzees. Analysis further showed that the HCV strains obtained from the patient in 1979 and 1990 had mutated from the 1977 strain. This change in viral strains may have accounted for the antibodies' inability to ward off the virus.

*Ref: Farci, P., et al., "Prevention of Hepatitis C Virus Infection in Chimpanzees After Antibody-Mediated in vitro Neutralization," **Proceedings of the National Academy of Sciences**, Vol. 91, pp. 7792-7796, August 2, 1994.*

Hormonal Factors May be Linked to Stroke in Females

Low estrogen appears to escalate the risk for subarachnoid hemorrhage, a type of stroke that disproportionately affects women. For female smokers, or those who previously smoked, hormone replacement therapy markedly reduces the risk, according to a study of more than 300 women of various ages supported by NIH's National Institute of Neurological Disorders and Stroke (NINDS).

Although the overall rate of strokes is higher in men, subarachnoid hemorrhage occurs twice as frequently in women. A subarachnoid hemorrhage develops when an aneurysm, a balloon-like sack on a blood vessel, bursts and bleeds into the space around the brain. Common risk factors for stroke, including cigarette smoking, excess alcohol consumption, and high blood pressure cannot explain the gender discrepancy for this type of stroke, since these factors are more common in men than women.

In looking for a possible assocation between hormonal factors and subarachnoid hemorrhage, Dr. W.T. Longstreth, Jr., and colleagues at the University of Washington School of Medicine and the School of Public Health and Community Medicine in Seattle matched each of 103 women who experienced this type of stroke with two randomly-selected healthy women of the same age.

Generally, women with lower estrogen, due either to postmenopausal status or other factors (e.g. smoking), were at higher risk for subarachnoid hemorrhage. Younger (menstruating) females and postmenopausal women taking estrogen replacement therapy were at decreased risk. Supplemental estrogen greatly reduced the risk of subarachnoid hemorrhage among current or former smokers.

One theory about the mechanism involved is that estrogens improve the overall cholesterol profile. This in turn reduces the risk for atherosclerosis (hardening of the arteries), a risk factor for aneurysm formation. Estrogens have also been associated with decreased blood pressure, which equates to a lower risk of aneurysm formation and rupture. Finally, there may be an overall health-promoting effect of estrogen on blood vessels, according to Longstreth, perhaps lessening the threat for this type of stroke in women.

The scientists conclude that the woman at greatest risk for subarachnoid hemorrhage is a smoker, younger than 65 years of age, who had an early menopause and has never taken estrogen supplements.

Ref: Longstreth, W.T., Jr., M.D., et al., "Subarachnoid Hemorrhage and Hormonal Factors in Women," ***Annals of Internal Medicine****, Vol. 121, No., 3, pp. 168-173, Aug. 1, 1994.*

Electroconvulsive Therapy (ECT) Does Not Cause Brain Damage

A major review of both humans and animals receiving electroconvulsive therapy (ECT) has concluded that there is no credible evidence that the procedure produces structural brain damage. These findings were reported by scientists supported by NIH's National Institute of Mental Health (NIMH).

ECT, in which electricity is passed through the brain to elicit a seizure, has long been known to help reduce symptoms of severe depression and schizophrenia. ECT has also been used less often to treat epilepsy and several other brain-related disorders.

Although ECT is safer today than in previous years, (anesthesia and muscle relaxants are currently used during the procedure), many still fear the technique, in part due to the stigma associated with the procedure, its invasive nature, and possible side effects. These may include memory loss and possible structural brain damage.

Investigators, led by Dr. D.P. Devanand from the New York State Psychiatric Institute and Columbia University, conducted a comprehensive literature review of studies involving both animals and humans. Their findings indicated that ECT does not result in serious, lasting cognitive changes. Some spotty memory loss, difficulties in recent memory and in retaining newly-learned information, often occurs following ECT, but these symptoms usually fade as time from treatment increases.

Overall, CT (computerized tomography) and MRI (magnetic resonance imaging) scans drawn from the literature showed that ECT did not produce structural brain changes. Early animal studies which suggested lasting, deleterious brain effects attributable to ECT were for the most part poorly controlled or had other methodological shortcomings, the researchers found. In addition, the epilepsy literature indicated that prolonged, intensive seizure activity, far in excess of that observed clinically during ECT, is required to produce structural brain damage.

*Ref: Devanand, D.P., et al., "Does ECT Alter Brain Structure?," **American Journal of Psychiatry**, Vol. 151, No. 7, pp. 957-967, July 1994.*

Urinary Incontinence and Mortality: Is There a Connection?

Contrary to earlier reports, urinary incontinence—the involuntary loss of urine—does not contribute to or predict death, findings from a study of community-dwelling men and women indicate. The investigation of nearly 2,000 individuals was conducted by scientists supported by NIH's National Institute on Aging.

While urinary incontinence can be embarrassing, often limits activity, and may promote urinary infections, some previous evidence suggests it may also be linked to mortality. Urinary incontinence affects a large number of institutionalized adults and about 30 percent of elderly individuals who reside in the community.

To determine whether an association exists between urinary incontinence and death, Drs. A. Regula Herzog, Ananias C. Diokno, and colleagues from the University of Michigan, in Ann Arbor, gathered data from a 6-year study involving a representative sample of 1,956 community-residing persons who were 60 years or older at the beginning of the project. Residents received an initial interview, then were reinterviewed annually for each of the next 3 years. Participants were initially identified (at baseline exam) as either continent or incontinent (uncontrolled urine loss within the 12 months prior to interview). Reassessments of continent status were also made at follow-up interviews.

After controlling for factors such as age, overall health, and education, Herzog and her colleagues found that there was no link between urinary incontinence and death—specifically, the condition had no effect on 6-year mortality among these community-dwelling individuals.

*Ref: Herzog, A.R., et al., "Urinary Incontinence as a Risk Factor for Mortality," **Journal of the American Geriatrics Society**, Vol. 42, No. 3, pp. 264-268, March 1994.*

Repeated Cyanide Exposure May Affect Brain

Moderate, chronic exposure to cyanide, a commonly-used industrial compound, may cause cellular damage and lesions to the brain, characteristic of what might be seen in Parkinson's disease. These findings emerge from animal studies conducted by investigators supported by NIH's National Institute of Environmental Health Sciences (NIEHS).

Cyanide is regularly used in the metal-processing industry. The substance also is found in cigarettes, as well as the pits of apples, peaches and apricots, but generally in amounts too low to cause harm.

However, some industrial workers are typically exposed to cyanide on a regular sustained basis, and some experts suspect this could alter brain function. Evidence from early animal studies suggests it may cause a loss of key brain chemicals.

Researchers with Purdue University in West Lafayette, IN, treated mice with moderate doses of cyanide twice a day for a week, amounts thought relatively comparable to those received by some industrial workers. Sixteen hours after the last dose was given, various measures of brain chemicals, blood, and behavior were taken and compared to the same measures in control mice treated with a salt solution.

Dr. Gary E. Isom and his Purdue University colleagues found that dopamine levels were significantly depleted in the treated mice due to a loss of key brain cells. In some parts of the brain dopamine levels declined by as much as 41 percent. Such changes did not occur in the controls.

Dopamine is a neurotransmitter or brain chemical that, among other things, helps regulate movement. Mice treated with cyanide for longer periods of time experienced noticeable motor control deficits, such as incoordination. These effects were not however seen in mice only briefly exposed to the agent.

The mobility impairment seen in the cyanide-treated mice mimic, in part, some symptoms seen in Parkinson's disease, leading the researchers to suggest that chronic exposure to elevated levels of cyanide may be a health hazard.

Ref: Kanthasamy, A.G., et al., "Dopaminergic Neurotoxicity of Cyanide: Neurochemical, Histological, and Behavioral Characterization," ***Toxicology and Applied Pharmacology,*** *Vol. 126, pp. 156-163, 1994.*

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NIH NEWS & FEATURES

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New Evidence On Loud Sounds Likely to Assist Hearing Impaired

BY JO BAGLEY

New findings about how the brain determines the loudness of sounds could benefit many of the millions of Americans who have hearing impairments. The findings, reported by scientists funded by NIH's National Institute on Deafness and Other Communication Disorders (NIDCD), show that two mechanisms, rather than one, help the brain determine variations in loudness.

This advance should help improve the design and function of prosthetic hearing devices such as cochlear implants and hearing aids, which are currently used by millions of adults and children in the United States.

The research was conducted by Drs. Fan-Gang Zeng and Robert V. Shannon of the House Ear Institute in Los Angeles, CA.

Auditory implants (both cochlear and brain stem) are designed to aid hearing by bypassing damaged portions of the inner ear, or the auditory nerve. With cochlear implants, electrodes are surgically implanted in the cochlea of persons with profound hearing deficit due to a damaged cochlea. The cochlea is a spiral-shaped organ within the inner ear that contains auditory nerve endings. These implants attempt to perform the function of the cochlea by sending a man-made electrical signal directly to the auditory nerve.

Electrodes of brain stem implants are surgically implanted in the brain stem of individuals with profound hearing impairments to bypass a damaged auditory nerve. These implants send a man-made electrical signal to the brain.

"Cochlear and brain stem implants successfully restore partial hearing to many individuals with profound hearing impairment," said Zeng. "The devices usually help wearers detect sounds around them, but are not adequate to help them understand speech by hearing alone," he added. One of the critical factors in the design of these implants is the transformation of sound energy into an electrical signal that the brain can use to detect loudness.

The auditory system determines loudness through the cochlea of the inner ear, which transforms sound waves into electrical signals that are carried by the hearing, or auditory nerve, to the brain. Loudness, which is determined in the brain, is a person's judgment of the intensity of a sound.

Scientists have thought for some time that the cochlea not only transforms

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sound, but also begins processing sound to help the brain detect loudness variations. Until now, however, scientists were not aware that more than one mechanism was used to process loudness.

"Our research suggests that the loudness of very low pitched sounds is not coded in the cochlea," said Zeng. He added, "Low pitched sounds appear to be transformed in the cochlea and then travel along the auditory nerve to the brain stem, where they are processed. The loudness of pitches higher than 300 hertz (Hz), however, still appears to be primarily coded in the cochlea."

The research team tested loudness variations of several tones in a small group of adults: some with cochlear implants, others with brain stem implants. While patients with brain stem implants processed the loudness of all pitches the same, patients with cochlear implants processed the loudness of low pitches differently.

"We are not sure how and why this happens, but these results strongly suggest that two mechanisms code for loudness at two different levels of the auditory pathway. This knowledge could greatly enhance the design of both cochlear and brain stem implants," said co-researcher Shannon.

"It is now possible to design the cochlear implant so that it more closely performs the same function as the cochlea, at least in terms of loudness, which should help wearers better understand speech," Zeng explained. Cochlear implants should be designed so that lower pitched sounds are presented differently to the auditory nerve than higher pitched sounds. The same design, although untested, should also help improve the effectiveness of hearing aids, he added.

Although considerably more work is needed in this area, "this research demonstrates the valuable information that can be obtained by evaluating the processing abilities of patients with cochlear and brain stem implants," said Dr. James B. Snow, Jr., Director, NIDCD. "This work will not only improve the capabilities of hearing devices, it may lead the way for further research that will improve our understanding of sound perception," he concluded. ▲

This research was published in the April 22, 1994 issue of **Science.**

Jo Bagley is a technical writer/editor with NIH's National Institute on Deafness and Other Communication Disorders.

Strict Glucose Control Inhibits Eye, Kidney Complications in Adolescents With Diabetes

Intensive treatment and close monitoring of insulin-dependent diabetes (IDDM) in adolescents can help avert or postpone some of its debilitating, long-term complications—including diabetic retinopathy (retinal disease), the leading cause of blindness in young adults, and nephropathy (kidney disease), according to scientists supported primarily by NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Earlier results from this study of 1,441 patients, the Diabetes Control and Complications Trial (DCCT), showed that intensive treatment also markedly lowered the likelihood of complications in adults.

Subjects were all participants in the Diabetes Control and Complications Trial, a 10-year, multicenter clinical trial. In this segment of the study, the researchers randomly assigned 125 adolescents (13–17 years old at the start of the trial) with IDDM but no retinopathy (primary prevention group) and 70 adolescents with IDDM and mild retinopathy (secondary intervention group) to one of two therapeutic approaches: conventional treatment, with the goal of avoiding extremely high or low blood sugar levels; and intensive management—trying to achieve glucose levels as close to normal as possible.

Those assigned to conventional treatment took one or two daily insulin injections and performed blood-glucose monitoring once a day. Subjects placed on the intensive management protocol received at least three daily insulin injections or used an external insulin pump (which automatically releases insulin as needed), and more frequently monitored their blood sugar levels. Participants were followed for an average of nearly 7 ½ years.

Results indicated that adolescents from the primary prevention group who received intensive therapy decreased their risk for retinopathy by 53 percent, compared to those who followed conventional treatment. Teens from the secondary intervention group following intensive therapy lessened their risk of progression of retinopathy by 70 percent; in addition, microalbuminuria (protein in the urine), an early indicator of kidney disease, was reduced by 55 percent.

Although patients in the primary prevention group experienced nearly three times as many episodes of severe hypoglycemia (low blood sugar) as those in the conventional treatment group, the investigators emphasize that the benefits of intensive therapy still greatly outweigh the health risks of tight glucose monitoring in adolescents. Working closely with a team of health care professionals may help reduce the occurrence of hypoglycemic events in young patients, note the researchers.

Nearly 12,000 children and teenagers are newly-diagnosed with diabetes each year, according to the NIDDK.

Ref: "Effect of Intensive Diabetes Treatment on the Development and Progression of Long-Term Complications in Adolescents with Insulin-Dependent Diabetes Mellitus: Diabetes Control and Complications Trial," the Diabetes Control and Complications Trial Research Group, ***The Journal of Pediatrics****, Vol. 125, No. 2, pp. 177-188, Aug. 1994.*

Excessive Dietary Protein Intake Found to Shorten Survival Time in Men With Kidney Disease

Scientists funded by NIH's National Institute on Aging (NIA) have found that excess dietary protein intake may hasten death in older, Causcasian males with signs or symptoms of kidney disease.

High blood pressure and a high intake of dietary protein are generally thought to contribute to deteriorating renal function for individuals with kidney disease. Many experts contend that adequate control of blood pressure and protein restriction may slow the course of the disease.

To document the effect of protein consumption on survival in patients with and without indicators of kidney disease (e.g., protein in the urine, kidney stones), an investigation was conducted by Dr. Johanna T. Dwyer and colleagues at the Tufts University Medical School in Boston and the USDA Jean Mayer Human Nutrition Research Center on Aging, also at Tufts. The researchers obtained data from nearly 2,600 elderly men and women, (ages 65 to 74), 175 of them diagnosed with kidney disease. They were participants in the long-term National Health and Nutrition Examination Survey I (NHANES I) which began in 1971. The randomly selected noninstitutionalized individuals were followed for an average of 14.5 years.

Protein intake, one of the key variables looked at by Dwyer and her team, was determined from each subject's 24-hour recall of foods consumed. After accounting for other possible factors that could seriously compromise health and lead to early death, such as diabetes and high blood pressure, the researchers found that white men with kidney disease indicators who ate an extra 15 grams of protein a day (the equivalent of a small hamburger) were at 20 percent greater risk of death from kidney disease or any disorder, when compared to healthy controls. No effects on mortality attributable to protein intake were observed in women or in healthy people of either sex.

Because of the relatively small sample of patients with kidney disease, the researchers call for additional studies to further substantiate their findings.

Ref: Dwyer, J.T., DSc., RD, et al., "Diet, Indicators of Kidney Disease, and Later Mortality Among Older Persons in the NHANES I Epidemiologic Follow-Up Study," ***American Journal of Public Health****, Vol. 84, No. 8, pp. 1299-1303, Aug. 1994.*

Bereaved Caregivers: How Well Do They Adjust?

How well do caregivers adapt after the loss of a loved one? A new study sponsored by NIH's National Institute of Mental Health shows that the emotional stress and depression experienced during the caregiving years frequently linger—in some cases for as long as three years after the event.

Solid data are available on the health consequences of caregiving. It is well documented that caring for a terminally or chronically ill relative, such as one with dementia, has serious effects on the well-being of the caregiver. For instance, emotional disturbances such as clinically diagnosed anxiety or depression are quite common, affecting as many as 30 percent of caregivers participating in NIMH supported studies. But just how long do depressive symptoms remain after the death of the loved one? Little research has been done in this area.

Drs. Janice K. Kiecolt-Glaser, Ronald Glaser, and Joy C. Bodnar of the Ohio State University College of Medicine examined this issue in a long-term study involving 254 individuals; 98 continuing caregivers, 49 bereaved caregivers whose relative died between years 1 and 4 of the caregiving process; and 107 controls (non-caregivers).

The researchers found few differences in depressive symptoms between former caregivers and those still caregiving—both groups displayed high rates of depression, significantly greater than control subjects. Specifically, by year four, one out of three continuing caregivers were diagnosed with clinical depression, while nearly one out of four bereaved caregivers were similarly diagnosed. By comparison, fewer than one out of 10 controls were clinically depressed. *(Editor's note):* This clinical depression is not to be confused with the normal grief associated with the death of a loved one.

The study demonstrates that the psychological effects of caregiving often continue well beyond the caregiving years. In addition, earlier studies conducted by these and other researchers indicate that both former and current caregivers also typically undergo altered immune function. The researchers in the current study conclude that interventions should focus on treating former as well as current caregivers.

*Ref: Kiecolt-Glaser, J.K., Ph.D., et al, "Caregiving Depression After Bereavement: Chronic Stress Isn't Over When It's Over," **Psychology and Aging**, Vol. 9, No. 3, pp. 372-380, 1994.*

Link Drawn Between Alcohol Use and Infertility

Moderate alcohol consumption—one drink per day or less—may increase a woman's risk of infertility, say researchers supported by NIH's National Institute of Child Health and Human Development (NICHD), and the National Institute of Environmental Health Sciences (NIEHS).

While nearly one out of five married couples have experienced some problems with infertility, not much is known about how various factors, such as alcohol consumption, affect the ability to conceive. In a study of nearly 6,000 women, researchers from the Harvard School of Public Health and Brigham and Women's Hospital, both in Boston, assessed the relationship between fertility and alcohol use in women.

Led by Dr. Francine Grodstein, the investigators obtained self-reported data from women who gave birth, as well as from women evaluated at 7 infertility clinics. Nearly 1,900 infertile cases and over 4,000 women who had given birth were included in the final analysis.

After adjusting for other factors that could affect the results such as age and cigarette smoking, the researchers found a positive association between heavy alcohol consumption (more than the equivalent of 7 cans of beer a week) and infertility, due to ovulatory dysfunction.

Infertility due to problems with ovulation was about 30 percent more likely to occur in women who drank moderately, and about 60 percent more likely in women who drank heavily.

The scientists conclude that women who consume the equivalent of one drink a day or less may increase their risk of infertility due to ovulatory dysfunction.

Ref: Grodstein, F., ScD, "Infertility in Women and Moderate Alcohol Use," ***American Journal of Public Health****, Vol. 84, No. 9, pp. 1429-1432, Sept. 1994.*

Dizziness in Elderly May Have Psychological Component

Psychological problems such as depression and anxiety may cause or, more likely, contribute to chronic dizziness in older men and women, according to a study supported by NIH's National Institute on Aging (NIA).

Although dizziness has been associated with psychological illnesses such as panic disorder and anxiety in young and middle-aged adults, any possible relation between dizziness and emotional disturbances in older men and women has received little attention. Elderly individuals seldom receive psychological or psychiatric evaluations by their doctors when they report vertigo, or chronic dizziness.

To test the theory that psychiatric disorders may be underdiagnosed in a geriatric population with chronic dizziness, Dr. Philip D. Sloane and his associates from the Geriatric Dizziness Clinic at the University of North Carolina at Chapel Hill studied 56 patients with this disorder, and 68 healthy, age-matched volunteers (control subjects). Patients averaged nearly 76 years of age and had suffered from chronic dizziness for almost 4 years, on average.

All patients and controls received thorough physical and psychological evaluations. While only 3 patients were diagnosed with a primary psychological disorder leading to their symptoms, the investigators found that about one-third of the group had symptoms of emotional distress (mainly anxiety, depression, or a fear of falling) that contributed to their dizziness. In most cases, these patients also had a coexisting balance disorder. Far lower rates of psychological disturbance were found among controls.

Based on these findings, the researchers urge physicians to consider the possibility that psychological problems, which are treatable, may coexist with medical problems, when evaluating geriatric patients with chronic dizziness.

Ref: Sloane, P.D., et al., "Psychological Factors Associated with Chronic Dizziness in Patients Aged 60 and Older," ***Journal of the American Geriatrics Society****, Vol. 42, No. 8, pp. 847-852, Aug. 1994.*

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Targeted AIDS Education Needed for Mentally Ill

Severely mentally ill men and women suffer disproportionately high rates of HIV infection and AIDS, in part because these individuals generally misjudge their risk. These findings are drawn from a study funded by NIH's National Institute of Mental Health (NIMH).

Researchers, led by Dr. Michael D. Knox at the University of South Florida's Mental Health Institute in Tampa, rated knowledge about HIV and AIDS, HIV risk factors, and self-assessment of HIV risk among 120 predominantly white men and women undergoing hospital treatment for a mental illness. The average age of the subjects was about 32 and approximately half were men. Nearly half suffered from either schizophrenia or major depression; about one-third also had a substance abuse disorder.

Initially subjects were asked questions that would reveal their understanding about AIDS and HIV risk factors. Generally, participants showed good knowledge; for example, nearly 9 out of 10 identified condom use as a means for avoiding HIV infection. Nevertheless they often participated in health-endangering behaviors, despite being well-informed. More than one-third of the men said they never used a condom during sex, and only 15 percent said they used a condom for each sexual encounter. Further, 14 percent of the men and 16 percent of the women had engaged in anal intercourse. In addition, sharing needles was a common practice among those who participated in IV drug use, and nearly one-third of the subjects reported having sex while high on drugs or alcohol during the past year. Overall, nearly half of the patients were identified as being at medium to high risk for acquiring HIV, but only 12 percent saw themselves at that level of risk.

Individualized approaches to education and intervention are greatly needed to enable mentally ill men and women to fully comprehend their risk of acquiring HIV, according to the scientists. Attitudinal changes and efforts to encourage these individuals to use condoms, avoid needle-sharing, and refrain from having multiple sexual partners would serve as key risk-reduction strategies, they say.

Ref: Knox, M.D., Ph.D., et ol., "HIV Risk Factors for Persons with Serious Mental Illness," ***Community Mental Health Journal,*** *Vol. 30, No. 6, pp. 551-563, Dec. 1994.*

Folic Acid Offsets Side Effects of Arthritis Drug

Folate, a safe, inexpensive form of folic acid, a B vitamin, can help rheumatoid arthritis (RA) patients avoid the potentially toxic effects of methotrexate, a drug that helps reduce inflammation and other symptoms characteristic of the disease. The finding is from a

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study supported by NIH's National Center for Research Resources (NCRR).

Low doses of methotrexate decrease RA symptoms in patients, however many experience adverse reactions to the drug including gastrointestinal problems (e.g., nausea, mouth ulcers), blood and liver abnormalities, and loss of hair, and must withdraw from the medicine.

Anecdotal reports have suggested that folic acid helps patients avoid these side effects. To investigate this in a controlled setting, Dr. Sarah L. Morgan and her associates with the Birmingham Veteran's Administration Hospital and University of Alabama at Birmingham conducted a randomized, double-blind, placebo-controlled study in 79 RA patients, 19–78 years of age. The researchers assessed the impact of two different weekly doses of folic acid on the toxicity and efficacy of methotrexate. Specifically, patients were randomly assigned to receive either low-dose (5 mg. a week) folic acid, or a larger weekly dose (27.5 mg) of the supplement. The rest of the study participants were given placebos. Neither the patients nor the evaluators knew which therapy the patients received.

In evaluating their findings, the scientists assessed the safety of the methotrexate in all 79 patients, as well as prevalence of RA symptoms such as tenderness and swelling of the joints, and overall grip strength.

The researchers found that both folic acid groups experienced minimal toxic effects from methotrexate, which proved effective in relieving symptoms. The placebo group had significantly more side effects. In addition, the folic acid had no direct influence on the efficacy of the methotrexate.

Future studies will likely focus on determining the optimal folic acid dosage for this group of patients.

Ref: Morgan, S.L., M.D., R.D., et al., "Supplementation with Folic Acid During Methotrexate Therapy for Rheumatoid Arthritis. A Double-Blind, Placebo-controlled Trial," ***Annals of Internal Medicine****, Vol. 121, No. 11, pp. 833-841, Dec. 1, 1994.*

Self-Health Ratings by Older Diabetics Predictive of Mortality

Elderly individuals with diabetes who considered their health to be worse than that of their peers were twice as likely to die in the ensuing six years compared to those who viewed themselves at least as healthy as their age counterparts. The findings are from a large epidemiologic study supported by NIH's National Eye Institute (NEI).

The study, conducted by Drs. Erik J. Dasback, Ronald Klein, and associates at the University of Wisconsin-Madison, involved nearly 3,000 participants in the Wisconsin Epidemiology Study of Diabetic Retinopathy. Subjects were divided by age into two groups—patients diagnosed with diabetes before age 30 and thus taking insulin (younger onset), and a group of patients whose diabetes was diagnosed at 30 years of age or older (older onset). Of the latter cohort, 824 individuals were insulin-dependent, while 956 were not.

Participants underwent physical exams and ophthalmic evaluations and were also asked to assess their health compared to other people the same age. Seventy-three percent of the younger onset group rated their health as better or the same as others their age, while 26 percent said their health was worse (one percent did not know). The researchers found however, that overall, self-rated health did not accurately predict mortality in this group. Where it did, it could be explained by the presence of diabetic complications. In general, once the figures were adjusted for health status, younger subjects assessing their health as poor were no more likely to die than others in the following six years.

In contrast, the researchers found a distinct correlation between self-rating of health and death in the older onset group. More specifically, elderly patients rating their health as worse (or "don't know") than that of their age peers were twice as likely to die in the ensuing six years.

The investigators point out that these elderly patients may need a more thorough examination from their doctors, "to rule out the presence of a treatable condition," and, in an effort to encourage optimal care, urge physicians to view more seriously the self-health ratings of this particular population.

Ref: Dosbach, E.J., Ph.D., et al., "Self-Rated Health and Mortality in People with Diabetes," ***American Journal of Public Health****, Vol. 84, No. 11, pp. 1775-1779, Nov. 1994.*

Height Emerges as Risk for Hip Fracture in Males

Tall men—those six feet or over—have double the risk for a hip fracture, according to research supported by NIH's National Heart, Lung, and Blood Institute.

Although hip fractures more often affect aging women, they are not uncommon in men. To date, little inquiry has been made into the causes or risk factors for this traumatic injury in males.

Investigators analyzed 50,000 male health professionals, 40 to 75 years of age, taking part in the Health Professionals Follow-up Study. Initial baseline questionnaires were mailed to participants in 1986; follow-up questionnaires were distributed in 1988, 1990, and 1992. Data were analyzed by Dr. David Hemenway and his colleagues at the Harvard School of Public Health and Brigham and Women's Hospital in Boston, MA.

Among a number of factors that were assessed, the researchers found that only two were significantly related to the likelihood of hip fracture in this group of men–advancing age and tallness. Compared to men aged 40–44, for men aged 65–69 the likelihood of hip fracture was nearly 3 1/2 times higher; for men 70 and older, the risk was almost 4 1/2 times higher.

Further, it was found that after adjusting for age, men who stood 6 feet or taller were at slightly more than double the risk for a hip fracture than males less than 5 feet 9 inches. Future

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studies will attempt to define why tall men are more susceptible.

One out of every six elderly persons who suffers a hip fracture dies within one year of the accident. Many others are unable to walk again.

Ref: Hemenway, D., Ph.D., et al., "Risk Factors for Hip Fractures in US Men Aged 40 through 75 Years," **American Journal of Public Health**, *Vol. 84, No. 11, pp. 1843-1845, Nov. 1994.*

Clinical Questionnaire May Help Identify Patients at Risk for Suicide

General practitioners can now use a set of four basic questions to help determine if their patients are suicide risks, say scientists who devised the questionnaire. The researchers were funded by NIH's National Institute of Mental Health (NIMH) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Information taken from an NIMH survey of more than 6,000 individuals conducted in the 1980s enabled Dr. Lisa Cooper-Patrick and her colleagues at The Johns Hopkins Medical Institutions in Baltimore to identify clinical traits shared by individuals with suicidal
tion (thoughts). The researchers
ied their questionnaire around
nonly-shared risk factors for
le such as sleep problems, feelings
pression, worthlessness or guilt,
opelessness.

he four questions are: (1) Have
er had a period of 2 weeks or
when you had trouble falling
, staying asleep, waking up too
r sleeping too much?; (2) Have
er had 2 weeks or more during which you felt sad, blue, depressed, or when you lost interest and pleasure in things that you usually cared about or enjoyed?; (3) Has there ever been a period of 2 weeks or more when you felt worthless, sinful, or guilty?; (4) Has there ever been a period of time when you felt that life was worthless?

The questionnaire is needed, according to the researchers, because suicidal patients don't always appear depressed when visiting their doctor, nor do they always meet the clinical criteria for major depression or a psychiatric disorder of any kind. Although clinical depression was identified as a risk factor for suicidal tendencies in the NIMH study, only about one-third of suicidal patients actually met the criteria for major depression. Thus, if physicians asked about suicide of their patients who met only the criteria used to diagnose a mental illness or of those who appeared depressed, they would miss identifying a large segment of their patients who might commit suicide. The questionnaire could help counter this problem, and if a patient's responses indicated a high suicide risk, he or she could be referred immediately for psychiatric treatment, say the researchers.

The four-item test should supplement, not replace, clinical judgment, the researchers emphasize.

Some 30,000 people a year commit suicide in the United States.

Ref: Cooper-Patrick, L., M.D., et al., "Identifying Suicidal Ideation in General Medical Patients," **Journal of the American Medical Association**, *Vol. 272, No. 22, pp. 1757-1762, Dec. 14, 1994.*

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